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TRANSCRIPTIONAL ACTIVATION SYSTEM, ACTIVATORS, AND USES THEREFOR

Related Application

The present application is a Continuation-in-part of co-pending application number 60/017,016, filed May 3, 1996, the entire contents of which are incorporated herein by reference.

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Background of the Invention

Gene activation requires interaction of DNA-bound activators with proteins binding near the transcription start site of a gene (Ptashne, *Nature* 335:983, 1988). In eukaryotes, activation of RNA polymerase II genes requires many transcription factors in addition to RNA polymerase. Transcriptional activators have been shown to contact one or another of these transcription factors, including TATA-binding protein (TBP), TBP-associated factors (TAFs), TFIIB, and TFIIH (Roeder, *Trends Biochem. Sci.* 16:402, 1991; Zawel et al., *Prog. Nucl. Acids Res. Mol. Biol.* 44:67, 1993; Conaway et al., *Annu. Rev. Biochem.* 62:161, 1993; Hoey et al., *Cell* 72:247). Thus, it has been proposed that transcription initiation involves a multistep assembly process, various steps of which might be catalyzed by activators (Buratowski et al., *Cell* 56:549, 1989; Choy et al., *Nature* 366:531, 1993).

Some transcriptional activators are thought to recruit one or more transcription factors to the DNA, to cause crucial conformational changes in target proteins and thereby to facilitate the complex process of assembling the transcriptional machinery, or both (Lin et al., *Cell* 64:971, 1991; Roberts et al., *Nature* 371:717, 1994; Hori et al.,

Curr. Op. Genet. Dev. 4:236, 1994). Also, given the observation that yeast RNA polymerase II is associated with several transcription factors, in a complex termed the "holoenzyme", it has been proposed that some transcriptional activators might function by recruiting the holoenzyme complex to DNA (Koleske et al., *Nature* 368:466, 1994; Kim et al., *Cell* 77:599, 1994; Carey, *Nature* 368:402, 1994).

Transcriptional activation has been much studied both in the context of controlling gene expression in cells, for example so that principles of gene activation can be employed in genetic therapies, and as an experimental tool for analysis of protein-protein interactions in cells (Fields et al., *Nature* 340:245, 1989; Gyuris et al., *Cell* 75:791, 1993). One difficulty that has been encountered in the use and analysis of transcriptional activation systems, however, is that over-expression of transcriptional activators in cells typically inhibits gene expression, sometimes with dire results on the cells. This effect, termed "squelching", apparently represents the titration of a transcription factor by the over-expressed transcriptional activator (Gill et al., *Nature* 334:721, 1988). Another difficulty that has been encountered specifically in the protein-protein interaction applications is that useful controls are often unavailable, so that spurious results are often observed. Also, the protein-protein interaction systems are typically not useful for identification of proteins that interact with transcriptional activators themselves. Given that transcriptional activators represent a significant fraction of all known proteins, this limitation of existing systems presents a serious problem.

There remains a need for the identification of novel transcriptional activators and improved transcriptional activation systems. In particular, there is a need for strong transcriptional activators that do not "squelch" other known activators, and for protein-protein interaction systems useful for identifying interaction partners of transcriptional activators.

Summary of the Invention

The present invention provides novel transcriptional activators. In particular, the invention provides activators in which a short peptide having activating capability is linked to a DNA binding domain. The peptides do not correspond to fragments of known transcriptional activators (that is, their sequences are not found in the SwissProt database). Moreover, the peptides apparently activate transcription by a novel mechanism as they do not squelch known activators when they are over expressed in yeast. Without wishing to be bound by any particular theory, we propose that these activators function by interacting with a component of the RNA polymerase II holoenzyme; this hypothesis is consistent with the observation that the only other transcriptional activator known not to squelch is Gal11, which is part of the holoenzyme (see Barberis et al., *Cell*, 81:359, 1995). The present invention also provides methods of identifying, characterizing, and using such novel transcriptional activators. In particular, the invention provides methods of activating transcription by providing such a novel activator to a cell.

The present invention also provides novel transcriptional activation systems, each based on the idea of exploiting non-conventional transcriptional activators. The systems described herein utilize holoenzyme components, or factors that interact therewith, in a way that provides advantages over known transcriptional activation systems. For example, we provide protein-protein interaction systems that utilize Gal11 and/or Gal11P to overcome some of the above-mentioned difficulties with standard di-hybrid and interaction trap systems.

The present invention also provides novel TBP mutants that increase transcriptional activation by certain activators. The particular TBP mutants described enhance activation by Gal11 more than they enhance activation by Gal4 region II. The invention also provides methods of identifying, characterizing, and using such TBP mutants.

Description of the Drawings

Figure 1 [shows transcriptional activation by an inventive peptide activator, but not by peptides of the same composition but scrambled sequence] demonstrates the dependence between transcriptional activation and the order of amino acids in the inventive peptide activator, SEQ ID NO: 167. Peptides having the same composition as SEQ ID NO: 167, but different sequence orders, such as SEQ ID NO: 226 and SEQ ID NO: 227, produce substantially lower b-gal activity levels. As indicated, SEQ ID NO: 167 produces a β-gal activity level of 4400, while SEQ ID NO: 226 and SEQ ID NO: 227 produce β-gal activities of 100 and 17 respectively.

Figure 2 presents [β-galactosidase assays that demonstrate the contributions of certain Gal4-DNA binding domain residues to activation by peptide LS201] the results of β-galactosidase assays demonstrating how the inventive peptide activator, SEQ ID NO: 167, effects activity levels of mutagenized Gal4-DNA binding domain residues. The unmutagenized Gal4 DNA binding domain is represented by SEQ ID NO: 228; mutagenized domains are listed consecutively from SEQ ID NO: 229 through SEQ ID NO: 237.

Figure 3 shows transcriptional activation by [an inventive peptide] SEQ ID NO: 238, comprising Gal 4 residues 96-100 and SEQ ID NO: 201, when linked to the Pho4 DNA binding domain.

Figure 4 depicts the purification scheme used for yeast holoenzyme preparations.

Figure 5 shows *in vitro* transcriptional activation by Gal4-LS201 in a yeast nuclear extract.

Figure 6 shows *in vitro* transcriptional activation by Gal4-LS201 on the yeast holoenzyme.

Figure 7 is a schematic of a standard protein-protein interaction transcriptional activation assay.

Figure 8 is a schematic of a protein-protein interaction transcriptional activation assay employing Gal11 as the activation domain.

Figure 9 is a schematic of the "three-component" protein-protein interaction transcriptional activation assay.

Description of Preferred Embodiments

Novel Transcriptional Activators

Typical naturally-occurring transcriptional activators are modular proteins that have separable DNA binding and transcriptional activation regions (Ptashne, *Nature* 335:983, 1988). The present invention provides novel transcriptional activators, comprising a DNA binding moiety linked to a short, substantially hydrophobic peptide. The peptide is approximately 6-25 amino acids in length, and preferably is about 8-17 amino acids long. In particularly preferred embodiments, the peptide is 13 amino acids long.

The activating peptides of the present invention have amino acid sequences that do not correspond to a portion of a known transcriptional activation domain. Sequences of known transcriptional activation domains are available in the literature and in computer databases such as, for example, GenBank, PIR, SwissProt, NCBI, Prosite. One of ordinary skill in the art can therefore readily determine whether a particular peptide corresponds to a portion of a known activating region.

Preferred peptides of the present invention include at least approximately 25%, preferably at least approximately 50%, hydrophobic amino acids. That is, at least approximately 25-50% of the amino acid residues in preferred peptides of the present invention are alanine (A), leucine (L), isoleucine (I), valine (V), proline (P), phenylalanine (F), tryptophan (W), or methionine (M). Alternatively or additionally, preferred peptides include at least one aromatic residue (i.e., F, W, or tyrosine (Y)). Particularly preferred peptides also do not include any positively charged residues, at least not near the terminus farthest from the DNA-binding domain.

Particularly preferred peptides of the present invention are presented in Table 1 (identified with "LS"). Of the peptides presented in Table 1, those that, when expressed in yeast cells, activate β-galactosidase activity to at least about ½ the level observed with full-length Gal4 are preferred transcriptional activation peptides according tot he present

invention. For example, peptides LS4 (QLPPWL; SEQ ID NO: 8); LS8 (QFLDAL; SEQ ID NO: 16); LS11 (LDSFYV; SEQ ID NO: 21); LS12 (PPPPWP; SEQ ID NO: 23); LS17 (SWFDVE; SEQ ID NO: 33); LS19 (QLPDLF; SEQ ID NO: 37); LS20 (PLPDLF; SEQ ID NO: 39); LS21 (FESDDI; SEQ ID NO: 41); LS24 (QYDLFP; SEQ ID NO: 45); LS25 (LPDLIL; SEQ ID NO: 47); LS30 (LPDFDP; SEQ ID NO: 55); LS35 (LFPYSL; SEQ ID NO: 57); LS51 (FDPFNQ; SEQ ID NO: 71); LS64 (DFDVLL; SEQ ID NO: 85); LS102 (HPPPPI; SEQ ID NO: 92); LS105 (LPGCFF; SEQ ID NO: 95); LS106 (QYDLFD; SEQ ID NO: 97); LS120 (YPPPPF; SEQ ID NO: 115); LS123 (PLPPFL; SEQ ID NO: 118); LS135 (LPPPWL; SEQ ID NO: 136); LS136 (VWPPAV; SEQ ID NO: 138); LS152 (DPPWYL; SEQ ID NO: 154); LS153 (LY; SEQ ID NO: 156); LS158 (FDPFGL; SEQ ID NO: 160); LS160 (PPSVNL; SEQ ID NO: 162); LS201 (YLLPTCIP; SEQ ID NO: 167); LS202 (LQVHNST; SEQ ID NO: 169); LS203 (VLDFTPFL; SEQ ID NO: 171); LS206 (HHAFYEIP; SEQ ID NO: 175); LS212 (PWYPTPYL; SEQ ID NO: 183); LS223 (YLLPFLPY; SEQ ID NO: 195); LS225 (YFLPLLST; SEQ ID NO: 199); LS232 (FSPTFWAF; SEQ ID NO: 209); LS241 (LIMNWPTY; SEQ ID NO: 221) are preferred inventive peptides. Particularly preferred are those that activate at least approximately as well as does full-length Gal4 (e.g., LS4, LS11, LS12, LS17, LS19, LS20, LS35, LS64, LS102, LS123, LS135, LS136, LS160, LS201, LS206, LS223, LS225 AND LS203).

The peptides of the present invention can be linked to any available DNA binding moiety to create a transcriptional activator of the present invention. For example, the peptides can be linked to a DNA-binding polypeptide (e.g., an intact protein that does not function as a transcriptional activator but binds to DNA, or any portion of a DNA-binding protein that retains DNA-binding activity) (see, for example, Nelson, *Curr. Op. Genet. Dev.* 5:180, 1995), a DNA-binding peptide derivative (see, for example, Wade et al., *JACS* 114:8784, 1992; Mrksich et al., *Proc. Natl. Acad. Sci. USA* 89:7586, 1992; Mrksich et al., *JACS* 115:2572, 1993; Mrksich et al., *JACS* 116:7983, 1994), an anti-DNA antibody (see, for example, Stollar, *Faseb J.*, 8:337, 1994), a DNA intercalation compound (e.g., p-carboxy methidium, p-carboxy ethidium, acridine and ellipticine), a

groove binder (e.g., netropsinm, distamycin, and actinomycin; see, for example, Waring et al., *J. Mol. Recog.* 7:109, 1994), or a nucleic acid capable of hybridizing, to form a duplex or a triplex, with a target DNA sequence (see, for example Gee et al., *Am. J. Med. Sci.* 304:366, 1992). Preferably, the peptides are linked to a sequence-specific DNA-binding moiety, so that they can be targeted to a selected DNA site from which to activate transcription.

Any available linkage (e.g., covalent bonding, hydrogen bonding, hydrophobic association, etc.) may be utilized to associate the peptide to a DNA binding moiety, so long as the DNA-binding activity of the DNA-binding moiety and the transcriptional activation activity of the peptide are preserved. The linkage between the activating peptide and the DNA binding domain may be direct or may alternatively may be mediated by a "linkage factor". A linkage factor is any entity capable of mediating a specific association between the DNA binding moiety and the activating peptide while preserving the activities of both. The term "specific association" has its usual meaning in the art: an association that occurs even in the presence of competing non-specific associations. The concept of linkage factors is known in the field of transcriptional activation and its scope and significance will readily be appreciated by those of ordinary skill in the art. To name but one example, rapamycin acts as a linkage factor when it mediates interactions between a DNA binding moiety that includes, for example, FK506 binding protein and a transcriptional activating moiety that includes a cyclophilin (Belshaw et al., *Proc. Natl. Acad. Sci. USA* 93:4604, 1996).

Preferred transcriptional activators of the present invention comprise a small, substantially hydrophobic peptide as described above, linked to a DNA-binding polypeptide that preferably has sequence-specific DNA binding activity. In particularly preferred embodiments, the peptide is linked to the DNA binding domain (i.e., a sufficient portion of the protein to recognize DNA but not to have transcriptional regulatory activity in the absence of the attached peptide) of a transcriptional regulatory protein (see, for example, Klug, *Ann. NY Acad. Sci.* 758:143, 1995). The choice of DNA binding domain will of course depend on the gene intended to be activated; the DNA

binding domain should recognize a site positioned relative to the transcriptional start site of the gene that the activator can affect transcription. Preferably, the site should be within approximately 250-1000 basepairs of the transcription start site, although this is not strictly required as, particularly in higher mammalian systems (e.g., human), transcriptional activators are known to be effective when bound several thousand basepairs away (upstream or downstream) of the transcription start site (see, for example, Serneza, *Hum. Mutat.* 3:180, 1994; Hill et al. *Cell* 80:199, 1995).

The transcriptional activators of the present invention may be prepared by any available methods including, for example, recombinant nucleic acid methodologies (see, for example, Sambrook et al., *Molecular Cloning: a Laboratory Manual*, 2nd Ed., Cold Spring Harbor Press, Cold Spring Harbor, NY, 1989; Innis et al., *PCR Protocols: A Guide to Methods and Applications*, Academic Press, San Diego, Ca, 1990; Erlich et al., *PCR Technology: Principles and Applications for DNA Amplification*, Stockton Press, New York, NY, 1989, each of which is incorporated herein by reference), synthetic chemistry (see, for example, Bodansky et al., *The Practice of Peptide Synthesis*, Springer-Verlag, New York, NY, 1984; Atherton et al., *Solid Phase Peptide Synthesis: a Practical Approach*, IRL Press at Oxford University, England, 1989, each of which is incorporated herein by reference), or other techniques capable of linking the desired moieties to one another.

As described in Example 1, we prepared our transcriptional activators by using PCR to link random oligonucleotides, either 18 or 24 nucleotides long, to DNA encoding the Gal4 DNA binding domain, so that hybrid genes were produced that encoded a fusion protein consisting of a Gal4 DNA binding domain and either a 6-mer or 8-mer peptide. The hybrid genes were under control of a yeast promoter, so that the fusion proteins were expressed in yeast. We screened this library of potential transcriptional activators for those that could stimulate transcription of a β-galactosidase reporter gene that had upstream Gal4 binding sites, and also compared the activators' activity to that of full-length Gal4. After screening fewer than approximately 200,000 colonies, we had identified close to 200 activators. Thus, at least about 0.1% of our hybrid genes resulted

in fusion proteins with transcriptional activation activity; about 5% of these activators stimulated transcription more effectively that did full-length Gal4 (see Table 1). Particularly preferred transcriptional activators of the present invention, therefore, activate transcription at least as effectively as does a known activating region linked to the same DNA binding moiety as is employed in the novel transcriptional activator. Such transcriptional activators, that effectively stimulate transcription through an activation domain only approximately 6-8 amino acids long, have not previously been described.

We further characterized our new transcriptional activators by determining the nucleotide sequence of their hybrid genes, and deducing therefrom the amino acid sequence of the encoded proteins (see Example 1). Although we found no obvious consensus sequence among our activator peptides, we noticed that all were substantially hydrophobic. Specifically, each of the peptides had at least about 30% hydrophobic residues. The least hydrophobic peptides, LS106 and LS202, had 33% and 29% hydrophobic residues; the most hydrophobic had 100% hydrophobic residues (LS123, LS135, LS136, LS235). Overall, of 109 peptides sequenced, a total of 682 residues were analyzed, 466 of which (68%) were hydrophobic. Also, approximately 90% of the peptides we analyzed included at least one aromatic residue. Only one peptide LS215, had a basic residue. LS215 is one of the weaker activators we identified.

We have observed that certain residues of the Gal4 DNA binding domain to which our peptides are linked contribute to the observed transcriptional activation (see Examples 1 and 2). Specifically, we have found that, for at least the LS201 activator, deletion of any one of the last five residues (residues 96-100) of the Gal4 DNA binding domain reduces activation activity about 10-1000 fold. Furthermore, substitution of either Phe97 or Val98 with Ala also reduces transcriptional activation about 40-150 fold. On the other hand, substitution of either Gln99 or Asp100 with Val has no effect on transcriptional activation. Also, Gal4 residues outside of 96-100 are not required for transcriptional activation (see Example 2).

The results presented in Example 2 demonstrate that the present invention actually describes three different set of activator peptides: i) those listed in Table 1; ii)

peptides having an amino acid sequence identical to those listed in Table 1 except also including Gal4 DNA binding domain residues 96-100 (or 97-100); and iii) peptides having an amino acid sequence identical to those of set ii except that one or both of Gln99 and Asp100 has been substituted with another amino acid, preferably an Ala. Of these three sets, preferred activator peptides are those that stimulate transcription at least half as effectively as does full-length Gal4 in a side-by-side comparison, as described herein. Particularly preferred peptide activators of the present invention consist of Gal4 residues 96-100 (with or without substitutions at residues 99 and/or 100) plus either 6 or 8 additional, primarily hydrophobic residues. Accordingly, particularly preferred peptide activators are 11 or 13 amino acids long. Most preferred are 11- or 13- amino acid residues formed by linking one of the Table 1 peptides to Gal4 residues 96-100.

In order to further characterize our novel transcriptional activators, we assayed their ability to squelch activation by other transcriptional activators. A variety of natural activators, including a subset of mammalian transcriptional activators, have been observed to squelch transcriptional activation by Gal4 and Gcn4 when these natural activators are expressed in yeast (see, for example, Gill et al., *Nature* 334:721, 1988). Many of these activators have several acidic residues and have been called "acidic" transcriptional activators (see, for example, Ma et al., *Cell* 51:113, 1987). For the purposes of the present application, we define an "acidic transcriptional activator" as any activator that, when expressed in yeast, squelches activation by Gal4 and/or Gcn4. The squelching phenomenon is believed to result from competition by the activators (i.e., the test activator and Gal4 or Gcn4) for the same interaction target. If this model is correct, our data indicate that our novel transcriptional activators do not interact with the same target as do these acidic activators. Specifically, our new activators do not squelch activation by Gal4 (see Example 1).

As described in Example 1, we assayed the ability of our new transcriptional activators to squelch Gal4 activation by over-expressing the activators in a yeast cell. The specific method we employed is only one of many possible ways to overexpress a protein in yeast. In general, over-expression of transcriptional activators in yeast can be

accomplished, for example, by introducing the activator gene into the cells on a high copy-number plasmid such as a 2μ vector. Alternatively or additionally, the activator gene can be introduced into the cell after being linked to a promoter that naturally directs, or can be induced to direct, high levels of transcription in yeast. Exemplary high-expression promoters include Gal1/10, Adh, actin, etc.

Furthermore, similar squelching assays can be designed and performed to detect the ability of our transcriptional activators to interfere with the activity of any known transcriptional activator, in any desired experimental system. For example, we have tested our activators for their ability to squelch activation by Gal11, a protein that, when recruited to DNA through linkage to a DNA binding moiety, activates transcription as effectively as any known activator but does so through a mechanism distinct from that of the acidic activators and does not squelch their activity (see Barberis et al., *Cell* 81:359, 1995, incorporated herein by reference). As shown in Example 1, our new transcriptional activators do not squelch Gal11 activation. Thus, the present invention provides a novel class of transcriptional activators, unique in structure, activity characteristics, and method of identification. Each of these unique aspects is encompassed by the present invention.

We have also assayed the ability of our activator peptides to stimulate transcription *in vitro*. As described in Example 3, we find that an activator consisting of the Gal4 DNA binding domain (1-100) linked to peptide LS201 stimulates transcription in a yeast nuclear extract, and also appears to stimulate transcription in the presence of only the yeast holoenzyme. These findings lend support to our hypothesis that the present peptide activators constitute a novel class of transcriptional regulators that interact directly with the general transcription machinery.

One of ordinary skill in the art will readily appreciate that we have performed our transcriptional activator screen, and many of our analyses, in yeast primarily because of the simplicity of the system, and the demonstrated usefulness of information obtained from a yeast system in understanding mammalian, and particularly human, transcription. Many yeast transcriptional activators also function in higher systems, including human, and vice versa. The above-described screen for transcriptional activators can readily be

repeated in other systems (e.g., in mammalian cells, preferably human cells), by selecting reporter constructs that are expressed in the desired cell type, and by inserting the hybrid gene library into an appropriate expression vector (that is, into a vector that directs protein in the desired cell type) (see Example 4). Suitable expression vectors and reporter genes for a wide array of systems are well known in the art.

The novel transcriptional activators described herein are particularly useful for introduction into cells to stimulate transcription therein since these new activators, even when over-expressed, do not interfere with transcriptional activation by classical activators such as the acidic activators. These activators are therefore highly useful for all applications involving controlled gene activation.

The novel transcriptional activators of the present invention can be delivered to cells by any of a variety of available techniques. For example, where the DNA binding moiety consists of a polypeptide, the transcriptional activator can be delivered to the cells in the form of a gene linked to a promoter that is expressed in the cells. Techniques for gene delivery to cells are well known in the art and include transformation, transfection, electroporation, infection, etc. Where the DNA binding moiety does not constitute a polypeptide, or where the transcriptional activator is delivered to cells as an intact protein, the transcriptional activator can be delivered by means of known drug delivery systems such as lipid micelles, or any other available technique.

Particularly preferred uses of the transcriptional activators of the present invention are in gene therapy. Specifically, many diseases are known or proposed either to be caused by reduced expression of a particular gene, or to be alleviated by increased expression of a particular gene. For example, diabetes results from reduced expression of insulin, and many cancers are caused by mutation of tumor-suppressor genes. Many other diseases (including, e.g., cystic fibrosis) can also be treated be gene therapy. The present transcriptional activators can be employed to treat such diseases. Specifically, a transcriptionally activating peptide of the present invention is linked to a DNA binding domain that recognizes a site appropriately located relative to the relevant gene so that the activator is effective when bound to the site. The activator is then delivered to

appropriate cells by any available technique and is allowed to stimulate gene transcription. If desired, the activator can be provided to the cell as a gene under the control of a regulated promoter, so that expression of the activator in the cells can be controlled by exposure to an inducing agent. Such inducible promoters are well known in many systems. For example, useful human promoters include the glucocorticoid promoter, the NFκB promoter, the tetracycline promoter, or any other agent-responsive promoter. In one embodiment, the activator binding site is linked to a normal copy of a gene that is mutated in the cell. For example, where disruption of a gene results in a disease phenotype that is alleviated by introduction of a normal copy of the gene into the cell, the normal copy of the gene can be linked to a binding site for one of out activators and introduced into the cell along with the activator.

The present invention therefore encompasses methods of activating transcription by providing a novel transcriptional activator to a cell and recruiting that activator to a promoter at which it activates transcription. In preferred embodiments of the invention, the activator is recruited to the DNA by virtue of its being covalently attached to a DNA binding domain. However, it is also possible that mere expression of the activating peptides of the present invention in a target cell will activate transcription if the activating peptides themselves have the ability to interact both with a target in the transcription machinery and with another factor that recruits them to the DNA.

By providing novel transcriptional activators, the present invention also provides methods of identifying factors that interact with these activators, for example by standard biochemical, immunological, and/or genetic methods, or by the improved methods described herein. Once an interaction partner (or partners) is identified, that partner can be used in similar interaction-type assays to identify additional novel transcriptional activators of the type described herein.

System for Identifying Protein-Protein Interactions

In addition to providing novel transcriptional activators and associated methods of production and use, the present invention provides improved transcriptional activation

systems for identifying and analyzing protein-protein interactions. As mentioned above, transcriptional activation systems have for several years been recognized as useful means for identifying interacting protein pairs. Such systems are often referred to as "two-hybrid" (see, for example Fields et al., *Nature* 340:245, 1989) or "interaction trap" (see, for example, Gyuris et al., *Cell* 75:791, 1993) assays.

The basic idea of these protein-protein interaction systems is exemplified in Figure 7. A first protein or protein portion (protein A in Figure 7), that does not itself stimulate transcription, is fused to a known DNA binding domain and the fusion product is expressed in a cell. The cell also contains a reporter construct in which the recognition site for the DNA biding domain is linked to a detectable reporter gene. A second fusion protein, in which a protein or protein portion that interacts with protein A (protein B in Figure 7) is fused to a transcriptional activation domain, is also expressed in the cell. Interaction between protein A and protein B recruits the transcriptional activation domain to the DNA so that transcription of the reporter construct is induced.

These protein-protein interaction systems have been used to identify interaction partners for known proteins by fusing the known protein to either the DNA binding domain or the transcriptional activation domain and introducing the resulting fusion into cells along with a library fused to the other of the activation domain and the DNA binding domain. Typically, such assays are performed in yeast systems, with either β-galactosidase or a selectable marker (or both) as the reporter gene, but analogous systems have been developed in other cell types (see, for example, Vasavada et al., *Proc. Natl. Acad. Sci. USA* 88:10686, 1991; Fearon et al., *Proc. Natl. Acad. Sci. USA* 89:7958, 1992; Finkel et al., *J. Biol. Chem.* 268:5, 1993, each of which is incorporated herein by reference).

Many interacting protein pairs have been identified through the application of such systems (for reviews, see Fields et al., *Trends Genet.* 10:286, 1994; Allen et al., *Trends Biol. Sci.* 20:511, 1995, each of which is incorporated herein by reference), and standardized protocols can be found in readily available textbooks (see, for example, Shirley et al., *Methods Cell Biol.* 49:401, 1995, incorporated herein by reference).

Despite the success that has been achieved with known protein-protein interaction systems that rely on transcriptional activation, important drawbacks of the systems have also been identified (for discussions of drawbacks in reviews, see Fields et al., *supra*; Allen et al., *supra*). False positives are common. Moreover, these systems typically cannot be used to identify the interaction targets of transcriptional activators. Quite simply, if the activator is fused to the DNA binding moiety, the fusion activates transcription and the screen cannot be performed; if the activator is supplied as an activation domain, the assay typically still cannot identify interaction targets because the activator often cannot interact simultaneously with a DNA-bound version of its target and its target in the transcriptional machinery. Thus, interaction of the activator with its DNA-bound target precludes recruitment of the transcriptional machinery.

The present invention provides improved transcriptional activation systems for identifying protein-protein interactions. Figure 8 presents one embodiment of an improved transcriptional activation of the present invention. The improvement depicted in Figure 8 is that Gal11 is employed as the activator in a standard interaction trap or di-hybrid fusion assay. Thus, the target protein depicted in Figure 8 is preferably not a transcriptional activator (or other component of the transcription machinery that, when recruited to DNA through linkage with a DNA binding domain, activates transcription.

In the system presented in Figure 8, the DNA binding domain can be any DNA binding moiety that recognizes a known DNA sequence, but preferably corresponds to or includes a DNA binding domain of a known protein, most preferably of a transcriptional regulator for review, see Nelson, *Curr. Op. Genet. Dev.* 5:180, 1995. The most preferred DNA binding domains for use in these assays are the Gal4 (at least 1-100) and LexA(1-202) DNA binding domains.

The reporter gene utilized in the system of Figure 8 can be any gene whose expression is readily detectable. In yeast systems, preferred reporters include the β-galactoside gene and selectable genes such as *HIS3*, *LEU2*, *URA3*, etc.; in human systems, the preferred reporter genes are those for SV40 large T antigen used in CV-1 cells; Vasvada et al., *Proc. Natl. Acad. Sci. USA* 88:10686, 1991), CD4, cell-surface

molecules that can be selected in a cell sorter, or drug-selectable markers (Fearon et al., *Proc. Natl. Acad. Sci. USA* 89:7958, 1992).

Use of Gal11 as the activation domain in protein-protein interaction systems has many advantages over existing approaches. First of all, Gal11 is the most powerful known yeast activation domain (Himmelfarb et al., *Cell* 43:1299, 1990, incorporated herein by reference). Thus, assays employing Gal11 are likely to be even more sensitive than are existing systems and therefore to be useful for detecting weaker protein-protein interactions than are currently observed.

Furthermore, Gal11 does not squelch activation by known acidic activators, even when it is expressed at high levels (Barberis et al., *Cell* 81:359, 1995, incorporated herein by reference). Use of Gal11 in the transcriptional activation systems described herein therefore avoids toxicity problems often associated with over-expression of strong transcriptional activators.

Without wishing to be bound by any particular theory, we propose that Gal11 does not squelch transcriptional activation by acidic activators because it activates transcription through a different mechanism than that employed by the acidic activators. Specifically, we propose that Gal11 is part of the yeast RNA polymerase II holoenzyme and activates transcription when it is recruited to DNA simply because it, in turn, recruits the rest of the transcriptional machinery (see Barberis et al., *supra*). The present invention therefore encompasses the finding that use of RNA polymerase II holoenzyme components as transcriptional activation domains improves protein-protein interaction systems that assay for transcriptional activation.

Any component of the RNA polymerase II holoenzyme, or any artificial sequence that interacts with the holoenzyme, can be tested for its ability to be used as the transcriptional activation domain in the improved protein-protein interaction systems of the present invention depicted in Figure 8. Recognizing that the literature includes differing descriptions of the RNA polymerase II holoenzyme, we define a "holoenzyme component" for the present purposes as any factor associated with the holoenzyme in a holoenzyme preparation that, when used in an *in vitro* transcription assay, responds to

addition of purified transcriptional activator (e.g. Gal4; see, for example, Koleske et al. *Nature*, 368:466, 1994).

As mentioned above, one of the advantages of using Gal11 or another component of the RNA polymerase II holoenzyme as the transcriptional activation domain in a protein-protein interaction assay of the type described herein is that such factors do not squelch other known activators. In light of this teaching, one of ordinary skill in the art will recognize that other transcriptional activators that do not squelch acidic activators, even though the other activators are not components of the RNA polymerase II holoenzyme, are useful in the improved transcriptional activation systems of the present invention. For example, the novel transcriptional activators described above can be employed in the transcriptional activation systems described herein.

Figure 9 presents another embodiment of an improved transcriptional activation system of the present invention, which embodiment we term the "three-component" system. In the three-component system of the present invention, a test protein is fused either to a non-Gal4 DNA binding domain or to Gal4(1-100), and an interaction target (e.g., a library) is fused to the other. Both fusion constructs are introduced into yeast cells carrying a mutant Gal11 that has gained the ability to interact with Gal4(1-100), and also carrying a reporter gene linked to the DNA binding site for the non-Gal4 DNA binding domain. Preferred embodiments employ the Gal11P allele (Himmelfarb et al., *Cell* 63:1299, 1990).

The Gal11P allele was first identified as a mutation that potentiated the activity of weak Gal4 derivatives (Himmelfarb et al., *Cell* 63:1209, 1990). We have since found that Gal11P is a gain-of-function mutation that confers onto Gal11 the ability to interact with the Gal4 dimerization domain found in Gal4(1-100) (Barberis et al., *Cell* 81, 359, 1995). Thus, in preferred embodiments of the three-component system of the present invention, interaction between the selected protein and its target recruits Gal4(1-100) to the DNA. Interaction between Gal11P and Gal4(1-100) then recruits the RNA polymerase II holoenzyme, thereby stimulating gene transcription (see Example 5). The affinity of the selected protein for its target correlates at least roughly with the observed

level of transcriptional activation (see Example 5; see also Estojak et al., *Mol. Cell. Biol.* 15:5820, 1995, Yibing Wu, Ph.D. dissertation, Harvard University, 1996, incorporated herein by reference).

The three-component system of the present invention does not require use of the Gal11P allele *per se*. For example, the original Gal11P mutant bore an Ile residue at position 342 (Himmelfarb et al., *Cell* 63:1299, 1990). Subsequent randomization of codon 342 revealed that substitution with other hydrophobic residues (e.g., Leu or Val, to a lesser extent Met or Thr) yields the Gal11P phenotype to different extents (Barberis et al., *Cell* 81:359, 1995). Any of these Gal11 derivatives is useful in the practice of the present invention. Furthermore, the general principle observed is readily generalizable. That is, the present invention teaches an improved protein-protein interaction system employing an RNA polymerase II holoenzyme component gain-of-function mutation where the gain of function comprises an ability to interact with a component to which other entities can be fused for the performance of a three-component screen as described herein. Any other appropriate holoenzyme component mutant could readily be employed in the practice of the present invention.

The three-component system of the present invention has many advantages over existing protein-protein interaction systems. The primary advantage is that use of the mutant holoenzyme component (e.g., Gal11P) system provides a straightforward control that can be used to distinguish "true" positives, that rely on recruitment of the transcription machinery to the promoter, from "false" positives produced sporadically by the system. For example, in a screen in which a selected protein (e.g., a transcriptional activator) is linked to Gal4(1-100) and a library is linked to the DNA binding moiety, "positive" library clones (i.e., those that encode a true interaction partner to the selected protein) are identified as those that result in transcriptional activation in a Gal11P cell but not in a Gal11 cell. Better yet, the screen is performed in a Gal11 cell that also contains the Gal11P gene under the control of a regulatable promoter. The screen is performed under conditions in which the Gal11P gene is expressed (since Gal11P is a dominant mutation, this expression effectively converts the cell to a Gal11P cell), and then the

same colonies are tested under conditions in which the Gal11P gene is not expressed. This strategy avoids the complication of having to isolate plasmids from individual Gal11P colonies transform them into Gal11 cells and re-test the new transformants.

Also, because the transcriptional activation in this system is via the "Gal11" mechanism, over-expression of the selected protein-Gal4(1-100) fusion will not squelch endogenous activators. Furthermore, in preferred embodiments of this three-component system, where the selected protein fused to Gal4(1-100) is a transcriptional activator, the system offers an additional built-in advantage. Specifically, the integrity of the Gal4(1-100) fusion can readily be tested by providing the cell with a second reporter construct, this one including Gal4 DNA binding sites, and detecting activation of that promoter by the fusion. One of ordinary skill in the art will readily recognize that this integrity control may be performed simultaneously with or separately from any protein-protein interaction screen. That is, the second reporter can be introduced into a cell with just the Gal4(1-100) fusion, or with any or all of the other constructs used in the full screen.

Applications of the improved transcriptional activation systems described herein are, of course, not limited to the identification of new protein-protein interactions. As is known for the standard di-hybrid and interaction-trap systems, such assays can usefully be employed to test the existence or dissect the specifics of a protein-protein interaction (see, for example, Fields et al., *Trends Genet.* 10:286, 1994; Allen et al., *Trends Bioch. Sci.* 20:511, 1995). For example, the significance of mutations, deletions, or insertions in different regions of the interacting components can be assayed by studying their effects on transcriptional activation in these systems. Techniques for producing such mutations, deletions, and insertions are well known in the art. The advantages described herein of being able to examine the significance of effects, for example by comparing results in Gal11P and Gal11 cells, are equally applicable to these types of assays.

Other Embodiments

One of ordinary skill in the art will readily recognize that the foregoing represents merely a detailed description of certain preferred embodiments of the present invention.

Various modifications and alterations of the compositions and methods described above can readily be achieved using expertise available in the art, and are within the scope of the following claims.

For example, as mentioned above, all of the assays described herein can be performed in any of a variety of cell types. Yeast cells are often selected as the most convenient for experimental manipulation, but even there, the variety of yeast strains that are available affords a wide range of opportunity for the practice of the present invention.

In some instances, it may be desirable to perform the assays of the present invention in cells whose capacity for transcriptional activation has been altered. For example, we have identified various dominant mutations in the yeast TBP protein that enhance the transcriptional activation potential of various yeast activators (see Example 6). Specifically, the N69R and V71R mutations of yeast TBP, when expressed from an ARS-CEN plasmid in otherwise wild type yeast, increase the observed transcriptional activity of G4RII' derivatives by 2-3 fold, and that of a Gal4-Gal11 fusion (form a site 1200 basepairs upstream of the transcription start) 12 fold. Use of such mutant TBPs in the assays described above may make the system more sensitive.

Examples

EXAMPLE 1: Identification and Characterization of Novel Transcriptional Activators

Materials and Methods

MEDIA, YEAST STRAINS, AND REPORTER/PLASMIDS: Rich (YPD) and synthetic complete (SC) yeast media were prepared as described (Rose et al., *Methods in Yeast Genetics*, Cold Spring Harbor Press, Cold Spring Harbor, NY, 1990, incorporated herein by reference). Yeast strain JPY9 was described in Wu et al., *EMBO J.* 1996. The genotype of JPY9 is *MATα, ura3-52, trp1Δ63, leu2Δ1, his3Δ200, lys2Δ385, gal4Δ11, gal80.* Yeast reporter plasmids pRY131Δ2μ, pRJR227, and pJP169 contain the reporter gene, *lacZ*, and various upstream activating sites: UASg of GAL-lacZ, five consensus 17mer GAL4 binding sites, and two LexA binding sites, respectively. These upstream activating sites are all 191 bp away from the TATA box (Yocum et al., *Mol. Cell. Biol.* 4:1985, 1984; Carey et al.,

Science 247:710, 1990). Reporter plasmids were integrated at the URA3 locus of yeast after *ApaI* digestion.

LIBRARY CONSTRUCTION: The following oligonucleotides were synthesized: oligo1 has 30 nucleotides paring the upstream of coding sequence of GAL4(1-100) in plasmid pRJR217 (Wu et al., *EMBO J.*, 1996); oligo2 contains 30 nucleotides paring downstream of GAL4(1-100) coding sequence, a stop codon, 24 random nucleotides, and 18 nucleotides paring the C-terminus of GAL4(1-100) coding sequence; oligo3 contains 30 bp paring the downstream of GAL4(1-100) coding sequence, a stop codon, 18 random nucleotides, and 18 nucleotides paring the C-terminus of GAL4(1-100+840-850) coding sequence. DNA fragments encoding GAL4(1-100)+X8 or GAL4(1-100+840-850)+X6 were then generated by PCR using primer pairs oligo1-2 and oligo1-3, respectively, and using plasmid DNA RJR217 encoding GAL4(100), and pRJR206 encoding GAL4(1-100+840-850), respectively, as template. These PCR fragments were co-transformed into S.*cerevisiae* strain JPY9::RJR227 using LiOAc method (Rose et al. *supra* 1990) along with a yeast expression vector, pRJR217, that was linearized with *NcoI* and *SalI*. The PCR fragments were integrated into the vector by homologous recombination (Lehming et al., *supra* 1995), yielding a library of yeast colonies.

ACTIVATION ASSAY: The yeast colonies, 2-3 days after transformation, were subject to X-gal filter assay (Rose et al., *supra* 1990). Blue colonies were selected, plasmids were rescued from these colonies and re-transformed into yeast strain JPY9:RJR227 and JPY9:RY131Δ2μ. β-galactosidase activities were then determined by X-gal filter assay and ONPG liquid assay (Rose et al., *supra* 1990).

SQUELCHING ASSAY: The plasmids encoding the activating peptides were transformed into the yeast strain YPY9:JP169 along with a plasmid encoding lexA(1-87)-GAL4(74-881), or lexA(1-87)-GAL11(141-1081). Both activating peptides and lexA-GAL4 or lexA-GAL11 are in the plasmids, driven by the actin promoter. Both plasmids have the Ars-Cen replicating origin. Because the activating peptide gene and the lexA-fusion genes are under the control of the same promoter, they should be produced at the

same level in yeast cells. The transformed cells were assayed for β-gal activity and compared with the cells that were transformed with lexA-GAL4 or lexA-GAL11 alone.

SEQUENCING: All plasmids encoding the activating peptides were sequenced using sequenase v2.0 kit from Amersham/USB.

ACTIVATION IN MAMMALIAN SYSTEM: The DNA encoding the yeast activating peptides was amplified by PCR and cloned into an mammalian expression vector, pcDNA3 (from Invitrogen). The resulting plasmids were co-transfected into HeLa cells along with a reporter plasmid pG5EC which encodes a chloroamphenicol acetyl transferase (CAT) gene driven by the minimal adenovirus *E1b* promoter bearing five upstream consensus 17 mers of GAL4 binding sites. The CAT activities were determined using [^{14}C] chloroamphenicol as substrate (Sambrook et al. Molecular Cloning: a Laboratory Manual, 2d Ed. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

Results

We constructed expression libraries that would produce a Gal4 DNA binding domain (either 1-100 or 100+840-850) fused to short, randomized peptides (6 or 8 amino acid residues in length). We transformed these libraries into a yeast strain containing a reporter plasmid that included Gal4 DNA binding sites. One reporter plasmid (pRJR227) contained five Gal4 17-mers upstream of the β-galactosidase gene; another (p4131Δ 2μ) contained a natural UAS_G upstream of the same gene. We selected blue colonies by X-gal filter assay, recovered plasmids from the yeast cells in these blue colonies, and re-transformed and re-screened these positive plasmids. From approximately 200,000 colonies screened, we obtained approximately 200 activators. Transcriptional activation by each of these activators was dependent on the presence of Gal4 binding sites in the reporter construct, indicating that activation is specific. The activation potential varied among the activators (see Table 1); several (~5%) activated better than did full-length Gal4.

We determined the nucleotide sequence of the inserts in our positive clones, and thereby determined the amino acid sequence of the transcriptional activators (see Table 1). Although no obvious consensus sequence emerged, we found that our peptide activation domains contained primarily hydrophobic and acidic residues. No basic residues were observed, except in one weak activator. Each of our peptide sequences was new-in that, no peptide correspond to a known sequence in the SwissProt database.

TABLE 1
Activators from Random Library GAL 1-100+840-850+X6

Plasmid	Sequence	SEQ ID NO	β-gal Activity (5X17 mers)		Net Charge
			Plate Assay	Liquid Assay	
RJR191	GAL4 1-881 (Full length)		+++	2350	
RJR182	GAL4 1-100+840-881		++	1739	
RJR217	GAL4 1-100		-	3	
RJR206	GAL4 1-100+840-850 (840 WTDQTAYNAFG 850)	1	±	41	
LS1	CCC CTC TTN NCN NCC CTC	2	++		
LS2	ATT CCG CCA CCG TAT TTC I P P P Y F	3 4	++		0
LS3	CTG CCC GGG TGT TTC TTC L P G C F F	5 6	++		0
LS4	CAG CTC CCC CCC TGG TTA Q L P P W L	7 8	++	1882	0
LS5	TAC TGG CCC TCC CCC TTC Y W P S P F	9 10	++		0
LS6	GAG TTC CCC TAT GAC TTG E F P Y D L	11 12	+		-2
LS7	ACC GCC GAA TTC CCC CTC T A E F P L	13 14	++		-1

LS8	CAA TTT CTA GAC GCA CTT Q F L D A L	15 16	+	1174	-1
LS9	ACA TTC CCT GAC CCC TTC T F P D P F	17 18	+		-1
LS10	ATC GGC CCA NCN CTT TTC	19	++		
LS11	TTG GAT TTT TCC TAC GTC L D F S Y V	20 21	+++	2196	-1
LS12	CCC CCA CCA CCC TGG CCC P P P P W P	22 23	+++	2109	0
LS13	CTC TTT GAA TGA GGA ACC L F E *	24 25	+		-1
LS14	CTG CTC GAC ATA CCT TTC L L D T 0 F	26 27	++		-1
LS15	CTC CCC GAC GCC TTT CTC L P D A F L	28 29	++		-1
LS16	CTC TTC CCC GAC CTC AAC L F P D L N	30 31	++		-1
LS17	TCT TGG TTT GAT GTC GAA S W F D V E	32 33	++	1961	-2
LS18	CTT GAA CCT CCG CCC TGG L E P P P W	34 35	++		-1
LS19	CAG CTA CCT GAT CTG TTC Q L P D L F	36 37	+++	1727	-1
LS20	CCT CTC CCA GAC CTC TTC P L P D L F	38 39	+++	2215	-1
LS21	TTC GAA TTC GAT GAT ATC F E F D D I	40 41	++	9814	-3
LS22	ACC TTT TTC GAT ACC CCC T F F D T P	42 43	+		-1
LS24	CAA TAC GAT CTA TTC GAT Q Y D L F D	44 45	++	1153	-2
LS25	CTA CCG GAC TTA ATT CTC L P D L I L	46 47	++	1229	-1
LS26	CCC CCC CTG GAT CCA TGG P P L D P W	48 49	++		-1

LS27	CAA TAC GAT CTA TTC GAT Q Y D L F D	50 51	++		-2
LS28	ACC TTG TGA CGC CAG AGC T L *	52 53	++		0
LS30	CTA CCA GAC TTC GAT CCA L P D F D P	54 55	+	886	-2
LS35	CTA ATC CCA TAC TCC CTG L F P Y S L	56 57	++	1825	0
LS40	TTT CCT GAC CTC TTC CCC F P D L F P	58 59	++		-1
LS41	CCT AAC CCC TTC CCA CTG P N P F P L	60 61	++		0
LS42	TTC TAG AAC ACA CCC CCG F *	62 63	±		0
LS43	CCC CCC CCC CAA TAT TTC P P P Q Y F	64 65	+		0
LS44	GAG GAC ACC CCC CCC TGG E D T P P W	66 67	±	552	-2
LS46	TTC CCC CCC CCC CCA TTC F P P P P F	68 69	++		0
LS51	TTC CCC CCA TTC AAC CAA F P P F N Q	70 71	+	950	0
LS52	CCC CTG TTC TGA CTC GGA P L F *	72 73	+		0
LS53	ACC GGT CCA CCA GAG CTA T G P P E L	74 75	+		-1
LS60	CTA ATC CCA TAC TCC CTG L I P Y S L	76 77	+		0
LS61	ACC TTC CCT TAC TCA CTG T F P Y S L	78 79	++		0
LS62	GGC AGC TTC GAA CTC CTC G S F E L L	80 81	+		-1
LS63	CTG GAA TAC CCC ACC ACC L E Y P T T	82 83	+		-1
LS64	AAT TTT GAT GAC CTA CTC	84	+++	1905	-2

	N F D D L L	85			
LS66	CTG GAC GTA TTT TCA CAC L D V F S H	86 87	++		-1
LS101	CAG CTA CCT GAT CTG TTC Q L P D L F	88 89	++		-1
LS102	CAC CCC CCC CCT CCC ATT H P P P P I	90 91	++	1158	0
LS104	CCC CTG TTC TGA CTC GGA P L F *	92 93	++		0
LS105	CTG CCC GGG TGT TTC TTC L P G C F F	94 95	++	2403	0
LS106	CAA TAC GAT CTA TTC GAT Q Y D L F D	96 97	+	1385	-1
LS107	GCT CTC CCG CCG TAC CTC A L P P Y L	98 99	+		0
LS108	TTC CTC CCC TCC CTT CCC F L P S L P	100 101	++		0
LS110	ATC CCT CTC CTC TGT CTC I P L L C L	102 103	±	122	0
LS111	ATG CTC CCT CCC TAC ATC M L P P Y I	104 105	++		0
LS114	CCC CCC TAC ATA TGG CCA P P Y I W P	106 107	++		0
LS115	GCG CTA TGG TAG CTA CCC A L W *	108 109	++		0
LS118	GAC CTC AAT ATT TTC TAG D L N I F *	110 111	++		-1
LS119	CTA CCC ATG ACN CCG TTC L P M T P F	112 113	+		0
LS120	TAC CCC CCG CCG CCC TTT Y P P P P F	114 115	+	1443	0
LS121	NNN CCC GTA GNN CNC TGG	116	++		
LS123	CCC CTT CCN CCT TTT CTT P L P P F L	117 118	+++	1892	0

LS125	CTC CCC ACC ATG CCC CTC L P T M P L	119 120	+		0
LS126	CTC TTC CTA CCA CCC ACC L F L P P T	121 122	+		0
LS129	ACC GCC GAA TTC CCC CTC T A E F P L	123 124	+		-1
LS130	ACC GAT TTC CTT CTG CTG T D F L L L	125 126	++		-1
LS131	GGA GAA TAT TTC CCC TTC G E Y F P F	127 128	++		0
LS132	TTT ATA GAT CCC CCT CTC F I D P P L	129 130	++		-1
LS133	CTA ATC CCA TAC TCC CTG L I P Y S L	131 132	++		0
LS134	CAA TAC GAT CTA TTC GAT Q Y D L F D	133 134	++		-2
LS135	TTA CCT CCC CCC TGG CTT L P P P W L	135 136	+++	3121	0
LS136	CTC TGG CCA CCT GCC GTA V W P P A V	137 138	+++	1829	0
LS140	CCA ACA AAC TTC TAC TGA P T N F Y *	139 140	+		0
LS142	CTA ATC CCA TAC TTC CTG L I P Y F L	141 142	+		0
LS147	ATC TGC GAG AGT TTC TTT I C E S F F	143 144	++		-1
LS148	GCG GAC CCG TGG CTA CTC A D P W L L	145 146	++		-1
LS149	GCG CAG TAC CCT TTC TTC A Q Y P F F	147 148	++		0
LS150	CCT CCG TCA TTC TTC GGC P P S F F G	149 150	++		0
LS151	CTT TCC AGC CTT CCC TTC P S S L P F	151 152	++		0
LS152	GAC CCA CCA TGG TAC CTT D P P W Y L	153 154	+	1783	-1

LS153	CTC TAC TAA TAA TAA GCA L Y *	155 156	+	1262	0
LS155	CCT ATC CCC GGT TTC ACT P I P G F T	157 158	+		0
LS158	TTT GAC CCC TTG GGC ATC F D P F G I	159 160	+	1856	-1
LS160	CCC CCC AGT GTG AAC CTC P P S V H L	161 162	+++	2891	0
LS161	CCA GAC AAC GTC CTA CCG P D N V L P	163 164	++		-1

Activators from Random Library GAL4 1-100+X8

Plasmid		SEQ ID NO	Net Charge	ß-gal Activity (in YAG_6)	
				X-gal	ONPG
RJR191	GAL4 (1-881, Full length)			+++	2804
RJR217	GAL4(1-100) (89KALLTGLFVQD100)	165		-	3
LS201	TAC CTT TTA CCA ACC TGT ATA CCT Y L L P T C I P	166 167	0	++++	4395
LS202	CTA CAA GTC CAC AAC AGC AGA TAG L Q V H N S T	168 169	0	++	1655
LS203	GTT CTT GAC TTC ACC CCT TTC CTC V L D F T P F L	170 171	-1	++	1128
LS205	CCC CTT ACC TAC CCC CTC GCC GGA P L T Y P L A G	172 173	0	+	325
LS206	CTC CTC GCC TTT TAC GAG ATA CCG L L A F Y E I P	174 175	-1	+++	1423
LS207	CCC CCT GAC ACC TAC ATC TTC	176	-1	+	

	TTA P P D T Y I F F	177			
LS208	CAA CTC AAC TAC CCA CTC GCC ATA Q L N Y P L A I	178 179	0	+	173
LS209	CTC GTA CTA CCC CAG CCG CAA CTC L V L P Q P Q L	180 181	0	+	
LS212	CCT TGG TAC CCT ACG CCG TAT CTG P W Y P T P Y L	182 183	0	++	811
LS215	TGG CTC CGA TCG TTC AGC GTT CCC W L R S F S V P	184 185	+1	±	187
LS217	CTT GAA CCA TCA CTA TAT ATG ATA L E P S L Y M I	186 187	0	+	
LS218	TGC ATC TTG TCC CAC CAC GCT CCT C I L S H H A P	188 189	0	±	
LS220	GAC CTC ACA TGC TGT TTT TGC CTC D L T C C F C L	190 191	-1	+	198
LS221	CCG TTT ATT GGC GGC CCT TAC GCA P F I G G P Y A	192 193	0	+	
LS223	TAC CTA CTA CCT TTC CTT CCG TAC Y L L P F L P Y	194 195	0	+++	2366
LS224	TAC CCC TGG TTT CCA GTC CCC TTA Y P W F P V P F	196 197	0	±	
LS225	TAT TTA CTA CCT CTC CTC TCC ACT Y F L P L L S T	198 199	0	+++	2714
LS226	CTC TCC ATT CAA CCC TAT TTT	200	0	±	

	TTT L S I Q P Y F F	201			
LS228	GCC CTA TTC TAC CTC CTC TAA AAG A L F Y L L *	202 203	0	+	419
LS230	CCN TGG CCC TAC TAT TTN CCG ATC P W P Y Y F P I	204 205	0	+	
LS231	CCG ATT TGG CAA TAT ACC ATT TTC P I W Q Y T I F	206 207	0	+	
LS232	TTA TCC CCC ACC TTT TGG GCA TTC F S P T F W AF	208 209	0	++	
LS233	GAC CCC CCC TAC GCC TAT ACT CTG D P P Y A Y T L	210 211	-1	+	126
LS235	CCT GCA CTC CTG TTT CCA TTC ATC P A L L F P F I	212 213	0	+	763
LS236	TTC ACC TAC GCT CTC CCC TTC CCC F T Y A L P F P	214 215	0	+	390
LS239	CTC TTA CCA CTG CCT CTC TTC CTC L F P L P L F L	216 217	0	±	
LS240	CTA TTC CCC TGG ACA TAC CAA CTT L F P W T Y Q L	218 219	0	+	
LS241	CTT ATT ATG AAC TGG CCT ACA TAT L T M N W P T Y	220 221	0	++	
LS243	TAT ATT TTC NCG CTG AGC TTA TCA Y I F ? L S F S	222 223			
LS244	CTA ACA CCC CTC CCC TCA TGG	224	0	+	

	CTA L T P L P S W L	225			

We investigated the importance of the hydrophobic and acidic residues in our peptide activation domains by performing site-directed mutagenesis on selected activators. In particular, we converted the I residue of activator LS201 to a R, and found that the formerly strong activator was converted to a weak one. This finding indicates that positive charge does not correlate with activation potential in our activators.

We also tested the importance of peptide sequence by scrambling the residues of the LS201 activator. As shown in Figure 1, such scrambling reduces activation potential about 44-260 fold.

We also performed "squelching" assays (Gill et al., *Nature* 334:721, 1988) with our activators. Specifically, we tested whether over expression of our activators affected transcriptional activation directed by LexA-fused activators from a template containing 2 LexA binding sites 141 base pairs upstream of a *Gal1-LacZ* gene fusion (pJP168). Each of the activators tested squelched activation by other of our activators; however, none of our activators squelched activation by either lexA-Gal4 or lexA-Gal11 (see Table 3). This finding suggests that our new transcriptional activators act through a target distinct from that contacted by either Gal4 or Gal11. Without wishing to be bound by any particular theory, we propose that our novel transcriptional activators stimulate transcription by contacting surfaces in the RNA polymerase II holoenzyme that are not contacted by other, known transcriptional activators. Thus, these novel transcriptional activators can be introduced into cells without deleterious effects on natural transcription activation mechanisms at work in those cells.

TABLE 2

Activating Peptides do not Squelch Activation by LexA-Gal4 or LexA-Gal11

Novel Activator	LexA-Gal4 Units of β-	% Activation	LexA-Gal11 Units of β-	% Activation

	Galactosidase Activity		Galactosidase Activity	
none	3216 ± 241	100	3450 ± 200	100
Gal4	520 ± 245	16	2504 ± 410	73
LS64	3306 ± 758	103	4153 ± 515	120
LS110	2785 ± 672	87	3518 ± 622	102
LS160	3383 ± 782	105	3833 ± 842	111
LS201	2842 ± 308	88	4288 ± 621	124

We investigated the role played by the DNA-binding domain residue immediately adjacent the peptide in our novel activators. Specifically, we deleted that residue, an aspartic acid, and tested the ability of the deletion derivatives to activate transcription on a template containing 5 Gal4 17mers upstream of a *Gal1-LacZ* gene fusion (pRJR227). We found that the alanine does participate in transcriptional activation (Table 3).

TABLE 3
Role of D^{100} in Activation by Gal4 (1-100)-Peptide Activators

Activator	β-galactosidase Activity in JPYP:RJR227
Gal4	2958
Gal4(1-100)	3
LS201	5288
LS201ΔD^{100}	207

LS164	1716
LS164ΔD^{100}	84

EXAMPLE 2: Analysis of DNA Binding Domain Residues that Contribute to Transcriptional Activation; Identification of Additional Novel Transciptional Activators

Materials and Methods

ANALYSIS OF CONTRIBUTING DNA BINDING RESIDUES: Activator LS201, described above in Example 1, was mutagenized according to standard techniques to delete or substitute one or more of Gal4 DNA binding residues 96-100. Transcriptional activation by the resulting proteins was assayed on the pRJR227, as described above.

LINKAGE OF ACTIVATOR PEPTIDE TO PHO4 DNA BINDING DOMAIN: An activating peptide consisting of activator LS201 and Gal4 DNA binding domain residues 96-100 was cloned onto the Pho4 DNA binding domain (residues 153-312, corresponding to Pho4Δ2) by PCR. The resulting construct was introduced into yeast cells and its activating capability was determined by assaying acid phosphatase activity in those cells, and comparing it to cells into which either full-length Pho4 or Pho4Δ2 was introduced. All methods were as described in Gaudreau et al., *Cell* 89:55, 1997 and Svaren et al., *EMBO J.* 13:4856, 1994).

Results

Gal4 DNA binding domain residues 96-100 were mutagenized in the context of a transcriptional activator comprising peptide LS201, and activation potential of the mutants was assayed on a template in which five consensus Gal4 17mers were positioned upstream of a *GAL1-LacZ* reporter gene. Gene expression was detected by analysis of β-galactosidase activity. The results are presented in Figure 2. As can bee seen, deletion of any one of Gal4 residues 96-100 reduced activation 10-2000 fold; substitution of either Phe97 or Val98 with Ala also significantly decreased activation. By contrast, substitution of either Glu99 or Asp100 with Ala had little or no effect on activation. Production of

each of the mutant protein was confirmed by gel shift from whole cell extracts (data not shown).

To analyze the role of DNA binding residues further, we asked whether a peptide consisting of activator LS201 and Gal4 residues 96-100 could activate transcription when linked to a different DNA binding domain. Specifically, we linked this peptide to the Pho4 DNA binding domain. We assayed the transcriptional activation capability of our new fusion protein by detecting its ability to stimulate expression of the *PHO5* gene, which encodes an acid phosphatase whose enzymatic activity can be analyzed according to known techniques (see Svaren et al., *EMBO J.* 13:4856, 1994). As shown in Figure 3, we found that the hybrid activator stimulated transcription as effectively as did full-length Pho4. We note that the fold activation shown in Figure 3 is misleadingly low due to unrelated acid phosphatase activity in yeast cells that contributes to a high background (e.g., that results in 30 units of activity when no functional activator is probided; see line re Pho4Δ2).

EXAMPLE 3: *In Vitro* Activation by Inventive Transcriptional Activators

IN VITRO TRANSCRIPTION WITH YEAST NUCLEAR EXTRACT: *In vitro* transcription with a yeast nuclear extract was performed as described by Wu et al., *EMBO J.* 3951, 1996. Specifically, yeast nuclear extract was prepared as described (Ponticelli et al., *Mol. Cell. Biol.* 10:2832, 1990; Ohashi et al., *Mol. Cell. Biol.* 14:2731, 1994). Transcription reactions (25 µl) contained 10 mM HEPES, pH 7.5, 10 mM $MgSO_4$, 5 mM EDTA, 10% glycerol, 2.5 mM dithiothreitol, 100 mM potassium glutamate, 10 mM magnesium acetate, 2% polyvinyl alcohol, 8 mM phosphoenolpyruvate, 0.62nM pG_2E4, 5.5 nM pGEM3Z (Promega), and 3 µl yeast nuclear extract, (60 mg/ml). Reactions were incubated with Gal4 protein form 10 min at 25 °C. Nucleoside triphosphates were then added to a final concentration of 1 mM and the reactions were allowed to proceed for an additional 60 min at 25 °C. Primer extension was performed using an oligonucleotide to the E4 coding sequence as described (Lillie et al.,*Cell*, 46:1043, 1986; Lin et al., Cell, 5:659, 1988).

IN VITRO TRANSCRIPTION WITH YEAST HOLOENZYME: Yeast holoenzyme was prepared as described in Koleske et al., *Nature* 368:466, 1994 and depicted in Figure 4. Recombinant TBP and TFIIE were added to the holoenzyme fraction to reconstitute transcriptional activity. Otherwise, reactions were as described above for yeast nuclear extract transcription.

Results

Activator LS201, fused to the Gal4 DNA binding domain, was assayed for its ability to activate transcription. Figure 5 shows transcriptional activation by the Gal4-LS201 protein on a template containing five consensus Gal4 17mers. The activator stimulated transcription when added in 1, 5, and 30 ng amounts; above those levels (100 ng), the activator squelched transcription. Similar results were obtained when the transcription was mediated by the yeast holoenzyme rather than a nuclear extract (see Figure 6). In these reactions, Gal4-LS201 activated transcription to levels comparable to those observed with Gal4-VP16. Squelching was again observed at high concentrations of Gal4-LS201.

EXAMPLE 4: Identification of Novel Transcriptional Activators in Mammalian System

Generally

We will by DNA synthesis extend a gene encoding the DNA binding domain of GAL4 (residues 1-100). The nucleotides will be added without regard to sequence at first, although as results indicate we may bias these sequences (see below). DNA molecules encoding the DNA binding domain fused to additional peptide sequences, attached to a strong promoter, will be transfected into mammalian cells bearing a fluorescent reporter. For example, a fusion gene encoding green fluorescent protein will be put under control of the minimal *E1b* promoter bearing upstream GAL4 binding sites. Such a reporter will be expressed when bound by an activator. A fluorescence activated cell sorting (FACS) machine will be used to isolate cells expressing the reporter at high

levels. We will use PCR to recover the sequence of the new activators. We predict that at least some of these new activators will work at very high efficiencies and yet will have no inhibitory effects on cells even when expressed at high concentrations (see below). We might then take our best activators and subject them to further rounds of peptide addition and screening to find even better activators. We describe the experiment in more details next.

Construction of Stable Reporter Cell Lines

We will use a vector encoding enhanced GFP (EGFP)-neomycin fusion protein as a reporter. EGFP fluoresces 35-fold more intensely and is also more soluble than wild type GFP. Expression of EGFP will allow us to use a FACS machine to separate out cells interest of, whereas the neomycin resistance gene will allow us to obtain our targets as stable cell lines. this double reporter can help us eliminate false positive clones while screening the random library.

The reporter plasmid will be constructed by PCR and restriction enzyme digestion-ligation. Starting from an expression vector, pEGFP-C1 (available from CLONTECH) which contains a selective marker, hygromycin resistance gene, we will fuse a neomycin resistant gene in frame to the C-terminus of EGFP. The DNA cassette, containing five 17 mers of GAL4 high affinity binding sites upstream of the minimal adenovirus E1bTATA promoter, will replace the CMV promoter. The resulting reporter plasmid, pG5EFO, will be transfected into a mammalian cell line (e.g. HeLa, CHO), and hygromycin resistant cells will be selected and cloned to generate the stable reporter cell lines. The reporter cells can be tested by PCR for plasmid integration and by transfection of the activator GAL4-VP16 plasmid for the reporter expression. The reporter cell lines will be maintained in hygromycin medium and should have no or little expression of EGFP and neomycin in the absence of activators.

Construction of Random Libraries

We will start by adding 8 random residues to GAL4(1-100) DNA binding domain. We will, if needed, extend the random peptide to isolate more potent activators

(see below). An oligonucleotide will be synthesized to contain the following: a restriction site, a stop codon (TGA), 24 random nucleotides, and 18 bases which match the 3' end of GAL4 (1-100). The DNA fragment encoding GAL4(1-100)+X8 will then be generated by PCR using this oligonucleotide and the 5' sequence of GAL4 as primers, and GAL4(1-100) DNA as a template. This PCR fragment will be purified by agarose gel purification, digested with the appropriate restriction enzymes, and ligated into the multiple cloning sites of the plasmid pcDNA3.1/Zeo (from Invitrogen), a high level mammalian expression vector containing Zeocin resistance gene as a selective marker. This ligation reaction will be transformed into the *E. coli* strain DH5α to generate a library of colonies containing eight random amino acids fused to GAL4(1-100). These colonies will be combined into many pools (~100), in case we use transient transfection to screen the activators (see below). The plasmids will be isolated from these pools, combined, and used to transfect the reporter cells. Theoretically, the library has to contain at least $20^8=2.6 \times 10^{10}$ primary colonies to cover all the possible sequences. This would be difficult to generate. Our results of yeast activating peptides, however, indicate that activating sequences occur much more frequently. Therefore, we should be able to find activators be screening 10^5 primary colonies. In addition, our results also suggest that residues in human activating peptides may be similar to that of yeast. We can construct a biased library: we will fuse eight residues of F, L, P, D, and T, as these are the most common in our yeast activating peptides, in random order to GAL4(1-100). We will then only need $5^8=3.9 \times 10^5$ to cover all the possibilities in this library.

Transfection and Activator Screening

We will transfect the plasmids isolated from the random library into the EGFP-neo reporter cells using the standard methods, such as lipofectAMINE (from Gibco BRL) or calcium phosphate. About 40 hours after transfection, the cells will be trypsinized and flowed through a FAC sorting machine. The cells expressing EGFP at high level can be isolated, and these cells will be replated in the medium supplemented with geneticin (G418) and Zeocin for selection of both activating plasmid and reporter expression. We

will maintain these cells in the same medium until individual clones form. These clones will be selected and passed as stable cell lines. In these experiments a GAL4(1-100) expression plasmid will be used as negative control, and GAL4(1-100)+VP16(411-455) (pGAL-VP) as a positive control The activating peptides will be amplified by PCR and recloned into the vector pcDNA3.1/Zeo. the resulting plasmid will be retransfected back into reporter cells to check plasmid linkage. The real activating peptides will be sequenced and the stronger activators will be selected to test their effect on classical activators in squelching assay.

Alternatively, we will try to use transient transfections to screen the mammalian activating peptides. Transient assays do not rely on the integrating efficiency of the plasmid library. Hence, it may be relatively easy for us to obtain the activating peptides. We will transfect the plasmids from different pools of the library and assay the EGFP reporter by FAC scan or by fluorescence microscopy. The activating plasmid pool will be retransformed into *E. coli,* and the colonies will be pooled at smaller size. The plasmids from the subpools will be transfected into the reporter cells. This process will be repeated until we find a single colony of activating plasmid.

Squelching Assay

We will use transient transfection to test effects of the activators isolated on classic activator VP16. We will cotransfect pGAL-VP and a reporter plasmid with or without the activating peptide plasmid into HELa cells. Here, we will use pG5ELuc containing a luciferase gene instead of EGFP-neomycin as a reporter plasmid because it is readily quantitated. We will harvest transfected cells ~40 hours after transfection and measure luciferase activity using a luminometer machine. We will also include pCMV-lacZ plasmid in our transient transfection assay. pCMV-laxZ encodes a constitutively expressed β-galactosidase which will be assayed and used as an internal control to normalize transfection efficiencies. This assay will allow us to determine if the peptide activators squelch VP16.

After screening these libraries, we expect to find some strong activators that activate transcription by a mechanism different from that of classical activators. We will, if necessary, randomly mutagenize the identified activator(s) at one or two positions(s), or add a few more random residues, and screen for better activators. One advantage of using the FACS sorting is that we can set a threshold to separate the cells expressing EGFP at a level higher than that of the activator we mutagenized. This may allow us to obtain even stronger activators. Such activators will be further characterized and used in studies of sequence specific gene activation.

EXAMPLE 5: Three-Component Transcriptional Activation System for Identifying Protein-Protein Interactions

Materials and Methods

SYSTEM AND CONSTRUCT: Interaction assay of the three-component transcriptional activation system is performed in yeast strain YW9603, which is derived from yeast strain YT6 (Himmelfarb et al., Cell 63:1699, 1990) by replacing GAL11 gene with a GAL11P allele (N342V) (Barberis et al., Cell 81.359, 1995), and integrating a reporter gene JPY169. The reporter JP169 bears two LexA binding sites 191 base pairs upstream of GAL1 TATA box, followed by LacZ gene. TBP-LexA fusion is expressed from the yeast ACT1 promoter. GAL4 derivatives were described in Wu et al., *EMBO J.*, 1996 (in press), specifically, a GAL4(1-100)+(840-881) fusion gene, and derivatives deleted from the 3' end, were constructed using the polymerase chain reaction (oligonucleotide sequences available on request). These proteins were expressed in yeast from low copy number ARS1/CEN4 plasmids from a fragment of the yeast actin promoter (666 bp 5' to the ATG of ACT1). All regions of plasmids that had been subjected to PCR were sequenced to ensure that the correct fusion construct had been made, and that no mutations had arisen during amplification.

SURFACE PLASMON RESONANCE SENSORCHIP PREPARATION: *In vitro* affinities are measured by Surface Plasmon Resonance, as described in Wu et al., *EMBO J.*, 1996 (in

press). Specifically, the dextran surface of Sensorchip CM5 was activated by two consecutive 40 µl injections of NHS/EDC (Pharmacia) at a flow rate of 2 µl per minute. Streptavidin (Sigma) was then coupled to the activated dextran by injecting 10 µl of 0.1 mg/ml solution in 10 mM NaOAc, pH 4.5 at a flow rate of 2 µl per minute. The excess of activated dextran was blocked by two consecutive 40 µl injections ethanolamine at a flow rate of 2 µl per minute. This procedure prolonged the activation and blocking time (from the usual 7 minutes to 40 minutes) so that the negative charges on the dextran surface was greatly reduced. A 50mer DNA oligo (sequence available upon request) carrying two consensus GAL4 binding sites was synthesized with a biotin group attached to the 5' end. It was annealed to its complementary oligo (without biotin) by heating to 75°C followed by slow cooling. The resulting double strand DNA carries two GAL4 binding sites and is biotinylated at one end. 10 µl of the biotinylated DNA (6.25 µg/ml) was injected to the streptavidin immobilized chip at a flow rate of 5 µl per minute. The average result of the procedure is that ~3000 RU's of streptavidin was immobilized and ~600 RU's of DNA was attached to the chip. After the first regeneration (by washing with 10 µl 0.1% SDS), the DNA bearing sensorchip becomes very stable and it could sustain many rounds of regeneration without significant changes in the baseline levels. This DNA bearing chip was used to capture GAL4 derivatives in such a conformation that the activating regions were uniformly presented and their interactions with other proteins were studied. In control experiments, GAL80, TBP and TFIIB did not bind detectably to the DNA bearing chip (data not shown). The amine coupling method published in the BIAcore manual (Pharmacia Biosensor AB, 1994) differs from ours as follows: in the published method, the activation of dextran surface by NHS/EDC, binding of ligand, and blocking of excess activated dextran by ethanolamine was each performed by a single injecting of 35 µl volume at a flow rate of 5µl/min. This method produced chips that, in our preliminary experiments, bound TBP and TFIIB significantly, probably because of the relatively large amount of negative charge remaining on the unactivated portion of the sensorchip.

PROTEIN-PROTEIN INTERACTIONS: The activators (GAL4 derivatives and other activating regions fused to GAL4 DNA binding domain) were first passed over the DNA-bearing chip. Typically 10 μl of 0.01 mg/ml protein solution (~1 μM) in HBS (10 mM HEPES pH 7.4, 150 mM NaCl, 0.0005% Surfectant P20, Pharmacia) were injected at a flow rate of 5 μl/min, and the DNA was saturated by the activators. This is indicated by the first increase of the RU value on the sensorgrams. Various proteins to be tested (e.g., TBP) were then injected (typically 20 μl of 1 mM solution in HBS at a flow rate of 5 μl/min), and their binding to the activating regions was indicated by the second increase of the RU value on the sensogram. The DNA bearing chip was then regenerated by washing with 10 μl of 0.1% SDS, a procedure that washes both proteins off the DNA, but leaves the DNA bearing chip intact. The baseline of the sensorgrams always comes back to the original level after each regeneration. A different activator was then injected to the same surface at the same concentration, and the DNA was once again saturated with the activators. As a consequence the same number of the molecules of the activators was immobilized to the chip each time. The protein to be tested (e.g., TBP) was once again injected and its binding to this activator was compared to that of the previous one. This comparison, we believe, is highly accurate because the exact same concentration of the same protein to be tested (e.g., TBP) was injected, and same number of molecules of activators was immobilized each time. GAL4 DNA binding domain alone was used as a negative control for each tested protein.

KINETIC EVALUATION: The apparent kinetic constants (k_{on} and k_{off}) of TBP, TFIIB and other tested proteins binding to various activators were the protein to be tested (e.g., TBP) was injected, followed by an injection of 10 μl 0.1% SDS to regenerate the sensorchip. The activator was injected at the same concentration in each sensorgram, but the protein to be tested (e.g., TBP) was injected 7 different concentrations in 2 fold serial increases (e.g., TBP was injected at 0.0625 μM, 0.125 μM, 0.25 μM, 0.5 μM, 1 μM, 2 μM and 4 μM). All of the injections were performed at a flow rate of 5 μl/min. A sensorgram of a blank buffer injection following the injection of the activator was subtracted from each of the 7 sensorgrams showing different concentrations of the tested

proteins (e.g. TBP) binding to the activator. The resulting sensorgrams corrected for the slow decay of the activators from the DNA. This correction in fact did not significantly change the calculated K_D's. The binding kinetics of all the interactions fit well to the first order kinetics model, and the k_{on} and k_{off} was solved using linear regression algorithm. The apparent equilibrium constant K_D was obtained by dividing k_{off} with k_{on}.

Results

We employed TBP and Gal4 region II' (G4RII'), as interaction partners in a three-component screen. Specifically, we fused TBP to the LexA DNA binding domain and fused G4RII' (as Gal4(840-881)) to Gal4(1-100). We introduced these constructs into Gal11 and Gal11P yeast cells bearing a reporter that included two LexA binding sites upstream of a *GAL1-LacZ* reporter construct. We compared the expression levels of the *LacZ* gene in Gal11 and Gal11P cells by plate assay. Our results are presented in Table 4.

TABLE 4

G4RII'-TBP Interaction Assayed in Three-Component Transcriptional Activation System

Gal4 Derivative	*In vitro* Affinity for TBP	Blueness on X-Gal plates
(1-100) + (840-881)	$6 \times 10^6\ M^{-1}$	+++
(1-100) + (840-857)	$2 \times 10^6\ M^{-1}$	+
(1-100) + nothing	$0 \times 10^6\ M^{-1}$	-

EXAMPLE 6: Production and Characterization of TBP Mutants that Enhance Transcriptional Activation:

The TBP mutations N69R and V71R were isolated from screening a TBP mutant library in yeast strain YW9510, derived from JPY9 by integrating reporter gene RY131 and expressing a GAL4 derivative GAL4(1-100)+(858-881)F869A (Wu et al, *EMBO J.*, 1996, in press). TBP-encoding plasmids in darker blue colonies on X-gal plates were

rescued and characterized, yielding the above mutations. β-galactosidase activity was measured in YW9510 carrying these mutant TBP's and wild type TBP's.

The results are presented below in Table 5:

TABLE 5
Transcriptional Activation by Gal4(1-100; 858-881)F869A in the Presence of TBP Mutants

TBP derivative	β-galactosidase units
Wild-type	53
V71R	121
N69R	125

These mutations were tested in a yeast strain expressing a LexA-GAL11 fusion protein and a reporter gene carrying two LexA sites 1,200 base pairs away from the GAL1-LacZ TATA box. The results are shown below in Table 6:

TABLE 6
Transcriptional Activation by LexA-Gal11 in the Presence of TBP Mutants

TBP derivative	β-galactosidase units
Wild-type	13
V71R	164
N69R	192

SEQUENCE LISTING

(1) GENERAL INFORMATION:

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(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: Gal4 residues 840-850

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Trp Thr Asp Gln Thr Ala Tyr Asn Ala Phe Gly
1 5 10

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: LS1 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

CCCCTCTTNN CNNCCCTC
18

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS2 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

ATTCCGCCAC CGTATTTC
18

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS2 amino acid sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Ile Pro Pro Pro Tyr Phe
1 5

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS3 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

CTGCCCGGGT GTTTCTTC
18

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS3 amino acids sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Leu Pro Gly Cys Phe Phe
1 5

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS4 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CAGCTCCCCC CCTGGTTA
18

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS4 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Gln Leu Pro Pro Trp Leu
1 5

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS5 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

TACTGGCCCT CCCCCTTC
18

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS5 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Tyr Trp Pro Ser Pro Phe
1 5

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS6 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

GAGTTCCCCT ATGACTTG
18

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS6 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Glu Phe Pro Tyr Asp Leu
1 5

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS7 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

ACCGCCGAAT TCCCCCTC
18

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS7 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Thr Ala Glu Phe Pro Leu
1 5

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS8 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

CAATTTCTAG ACGCACTT
18

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS8 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Gln Phe Leu Asp Ala Leu
1 5

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS9 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

ACATTCCCTG ACCCCTTC
18

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS9 amino acid sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Thr Phe Pro Asp Pro Phe
1 5

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS10 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

ATCGGCCCAN CNCTTTTC
18

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS11 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

TTGGATTTTT CCTACGTC
18

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS11 amino acid sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

Leu Asp Phe Ser Tyr Val
1 5

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS12 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

CCCCCACCAC CCTGGCCC
18

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS12 amino acid sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Pro Pro Pro Pro Trp Pro
1 5

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS13 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

CTCTTTGAAT GAGGAACC
18

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS13 amino acid sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

Leu Phe Glu
1

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS14 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

CTGCTCGACA TACCTTTC
18

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 5 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS14 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

Leu Leu Asp Thr Phe
1 5

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS15 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

CTCCCCGACG CCTTTCTC
18

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS15 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

Leu Pro Asp Ala Phe Leu
1 5

(2) INFORMATION FOR SEQ ID NO:30:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS16 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

CTCTTCCCCG ACCTCAAC
18

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid

(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS16 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

Leu Phe Pro Asp Leu Asn
1 5

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS17 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

TCTTGGTTTG ATGTCGAA
18

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS17 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

Ser Trp Phe Asp Val Glu
1 5

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS18 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

CTTGAACCTC CGCCCTGG
18

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:

(B) CLONE: LS18 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

Leu Glu Pro Pro Pro Trp
1 5

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS19 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

CAGCTACCTG ATCTGTTC
18

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS19 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Gln Leu Pro Asp Leu Phe
1 5

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS20 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

CCTCTCCCAG ACCTCTTC
18

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS20 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

Pro Leu Pro Asp Leu Phe

1 5

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS21 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

TTCGAATTCG ATGATATC
18

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS21 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

ACCTTTTTCG ATACCCCC
18

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS22 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

ACCTTTTTCG ATACCCCC
18

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS24 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

Thr Phe Phe Asp Thr Pro
1 5

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS24 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

CAATACGATC TATTCGAT
18

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS24 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

Gln Tyr Asp Leu Phe Asp
1 5

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS25 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

CTACCGGACT TAATTCTC
18

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS25 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

Leu Pro Asp Leu Ile Leu
1 5

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:

(B) CLONE: LS26 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

CCCCCCCTGG ATCCATGG
18

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS26 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

Pro Pro Leu Asp Pro Trp
1 5

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS27 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

CAATACGATC TATTCGAT
18

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS27 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

Gln Tyr Asp Leu Phe Asp
1 5

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS28 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

ACCTTGTGAC GCGACAGC
18

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS28 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

Thr Leu
1

(2) INFORMATION FOR SEQ ID NO:54:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS30 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

CTACCAGACT TCGATCCA
18

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS30 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

Leu Pro Asp Phe Asp Pro
1 5

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS35 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

CTAATCCCAT ACTCCCTG
18

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid

(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS35 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

Leu Phe Pro Tyr Ser Leu
1 5

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS40 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

TTTCCTGACC TCTTCCCC
18

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS40 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

Phe Pro Asp Leu Phe Pro
1 5

(2) INFORMATION FOR SEQ ID NO:60:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS41 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

CCTAACCCCT TCCCACTG
18

(2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS41 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

Pro Asn Pro Phe Pro Leu
1 5

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS42 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

TTCTAGAACA CACCCCCG
18

(2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS42 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

Phe
1

(2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS43 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

CCCCCCCCCC AATATTTC
18

(2) INFORMATION FOR SEQ ID NO:65:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS43 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

Pro Pro Pro Gln Tyr Phe
1 5

(2) INFORMATION FOR SEQ ID NO:66:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS44 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

GAGGACACCC CCCCCTGG
18

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS44 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

Glu Asp Thr Pro Pro Trp
1 5

(2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS46 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

TTCCCCCCCC CCCCATTC
18

(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS46 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

Phe Pro Pro Pro Pro Phe
1 5

(2) INFORMATION FOR SEQ ID NO:70:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS51 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

TTCCCCCCAT TCAACCAA
18

(2) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS51 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

Phe Pro Pro Phe Asn Gln
1 5

(2) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS52 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

CCCCTGTTCT GACACGGA
18

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS52 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

Pro Leu Phe
1

(2) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS53 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

ACCGGTCCAC CAGAGCTA
18

(2) INFORMATION FOR SEQ ID NO:75:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS53 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

Thr Gly Pro Pro Glu Leu
1 5

(2) INFORMATION FOR SEQ ID NO:76:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS60 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

CTAATCCCAT ACTCCCTG
18

(2) INFORMATION FOR SEQ ID NO:77:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS60 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

Leu Ile Pro Tyr Ser Leu
1 5

(2) INFORMATION FOR SEQ ID NO:78:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS61 DNA sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

ACCTTCCCTT ACTCACTG
18

(2) INFORMATION FOR SEQ ID NO:79:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS61 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

Thr Phe Pro Tyr Ser Leu
1 5

(2) INFORMATION FOR SEQ ID NO:80:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS62 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

GGCAGCTTCG AACTCCTC
18

(2) INFORMATION FOR SEQ ID NO:81:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS62 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

Gly Ser Phe Glu Leu Leu
1 5

(2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS63 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

CTGGAATACC CCACCACC
18

(2) INFORMATION FOR SEQ ID NO:83:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS63 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

Leu Glu Tyr Pro Thr Thr
1 5

(2) INFORMATION FOR SEQ ID NO:84:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS64 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

AATTTTGATG ACCTACTC
18

(2) INFORMATION FOR SEQ ID NO:85:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS64 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

Asn Phe Asp Asp Leu Leu
1 5

(2) INFORMATION FOR SEQ ID NO:86:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS66 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

CTGGACGTAT TTCACAC
18

(2) INFORMATION FOR SEQ ID NO:87:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS66 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

Leu Asp Val Phe Ser His
1 5

(2) INFORMATION FOR SEQ ID NO:88:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS101 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

CAGCTACCTG ATCTGTTC
18

(2) INFORMATION FOR SEQ ID NO:89:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS101 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

Gln Leu Pro Asp Leu Phe
1 5

(2) INFORMATION FOR SEQ ID NO:90:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS102 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

CACCCCCCCC CTCCCATT
18

(2) INFORMATION FOR SEQ ID NO:91:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS102 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

His Pro Pro Pro Pro Ile
1 5

(2) INFORMATION FOR SEQ ID NO:92:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS104 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

CCCCTGTTCT GACTCGGA
18

(2) INFORMATION FOR SEQ ID NO:93:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS104 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

Pro Leu Phe
1

(2) INFORMATION FOR SEQ ID NO:94:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS105 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

CTGCCCGGGT GTTTCTTC
18

(2) INFORMATION FOR SEQ ID NO:95:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS105 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

Leu Pro Gly Cys Phe Phe
1 5

(2) INFORMATION FOR SEQ ID NO:96:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS106 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

CAATACGATC TATTCGAT
18

(2) INFORMATION FOR SEQ ID NO:97:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS106 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

Gln Tyr Asp Leu Phe Asp
1 5

(2) INFORMATION FOR SEQ ID NO:98:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS107 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

GCTCTCCCGC CGTACCTC
18

(2) INFORMATION FOR SEQ ID NO:99:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS107 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

Ala Leu Pro Pro Tyr Leu
1 5

(2) INFORMATION FOR SEQ ID NO:100:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS108 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

TTCCTCCCCT CCCTTCCC
18

(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS108 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

Phe Leu Pro Ser Leu Pro
1 5

(2) INFORMATION FOR SEQ ID NO:102:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS110 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

ATCCCTCTCC TCTGTCTC
18

(2) INFORMATION FOR SEQ ID NO:103:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS110 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

Ile Pro Leu Leu Cys Leu
1 5

(2) INFORMATION FOR SEQ ID NO:104:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS111 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

ATGCTCCCTC CCTACATC
18

(2) INFORMATION FOR SEQ ID NO:105:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS111 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

Met Leu Pro Pro Tyr Ile
1 5

(2) INFORMATION FOR SEQ ID NO:106:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS114 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

CCCCCCTACA TATGGCCA
18

(2) INFORMATION FOR SEQ ID NO:107:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS114 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

Pro Pro Tyr Ile Trp Pro
1 5

(2) INFORMATION FOR SEQ ID NO:108:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS115 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

GCGCTATGGT AGCTACCC
18

(2) INFORMATION FOR SEQ ID NO:109:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 3 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS115 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

Ala Leu Trp
1

(2) INFORMATION FOR SEQ ID NO:110:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS118 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

GACCTCAATA TTTTCTAG
18

(2) INFORMATION FOR SEQ ID NO:111:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 5 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS118 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:

Asp Leu Asn Ile Phe
1 5

(2) INFORMATION FOR SEQ ID NO:112:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS119 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:112:

CTACCCATGA CNCCGTTC
18

(2) INFORMATION FOR SEQ ID NO:113:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS119 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:113:

Leu Pro Met Thr Pro Phe
1 5

(2) INFORMATION FOR SEQ ID NO:114:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS120 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:114:

TACCCCCCGC CGCCCTTT
18

(2) INFORMATION FOR SEQ ID NO:115:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS120 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:115:

Tyr Pro Pro Pro Pro Phe
1 5

(2) INFORMATION FOR SEQ ID NO:116:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS121 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:116:

NNNCCCGTAG NNCNCTGG
18

(2) INFORMATION FOR SEQ ID NO:117:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS123 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:

CCCCTTCCNC CTTTTCTT
18

(2) INFORMATION FOR SEQ ID NO:118:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS123 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:118:

Pro Leu Pro Pro Phe Leu
1 5

(2) INFORMATION FOR SEQ ID NO:119:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS125 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:

CTCCCCACCA TGCCCCTC
18

(2) INFORMATION FOR SEQ ID NO:120:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS125 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:

Leu Phe Leu Pro Pro Thr
1 5

(2) INFORMATION FOR SEQ ID NO:121:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS126 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:

CTCTTCCTAC CACCCACC
18

(2) INFORMATION FOR SEQ ID NO:122:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS126 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:

Leu Phe Leu Pro Pro Thr
1 5

(2) INFORMATION FOR SEQ ID NO:123:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS129 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

ACCGCCGAAT TCCCCCTC
18

(2) INFORMATION FOR SEQ ID NO:124:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS129 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:124:

Thr Ala Glu Phe Pro Leu
1 5

(2) INFORMATION FOR SEQ ID NO:125:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS130 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:125:

ACCGATTTCC TTCTGCTG
18

(2) INFORMATION FOR SEQ ID NO:126:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS130 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:126:

Thr Asp Phe Leu Leu Leu
1 5

(2) INFORMATION FOR SEQ ID NO:127:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS131 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:127:

GGAGAATATT TCCCCTTC
18

(2) INFORMATION FOR SEQ ID NO:128:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS131 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:128:

Gly Glu Tyr Phe Pro Phe
1 5

(2) INFORMATION FOR SEQ ID NO:129:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS132 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:129:

TTTATAGATC CCCCTCTC
18

(2) INFORMATION FOR SEQ ID NO:130:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS132 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:

Phe Ile Asp Pro Pro Leu
1 5

(2) INFORMATION FOR SEQ ID NO:131:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS133 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:

CTAATCCCAT ACTCCCTG
18

(2) INFORMATION FOR SEQ ID NO:132:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS133 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:

Leu Ile Pro Tyr Ser Leu
1 5

(2) INFORMATION FOR SEQ ID NO:133:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS134 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:

CAATACGATC TATTCGAT
18

(2) INFORMATION FOR SEQ ID NO:134:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS134 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134:

Gln Tyr Asp Leu Phe Asp
1 5

(2) INFORMATION FOR SEQ ID NO:135:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS135 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:

TTACCTCCCC CCTGGCTT
18

(2) INFORMATION FOR SEQ ID NO:136:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS135 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:

Leu Pro Pro Pro Trp Leu
1 5

(2) INFORMATION FOR SEQ ID NO:137:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS136 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:

CTCTGGCCAC CTGCCGTA
18

(2) INFORMATION FOR SEQ ID NO:138:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS136 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:138:

Val Trp Pro Pro Ala Val
1 5

(2) INFORMATION FOR SEQ ID NO:139:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS140 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:

CCAACAAACT CCTACTGA
18

(2) INFORMATION FOR SEQ ID NO:140:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 5 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS140 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

Pro Thr Asn Phe Tyr
1 5

(2) INFORMATION FOR SEQ ID NO:141:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS142 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

CTAATCCCAT ACTTCCTG
18

(2) INFORMATION FOR SEQ ID NO:142:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS142 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:

Leu Ile Pro Tyr Phe Leu
1 5

(2) INFORMATION FOR SEQ ID NO:143:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS147 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

ATCTGCGAGA GTTTCTTT
18

(2) INFORMATION FOR SEQ ID NO:144:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS147 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:144:

Ile Cys Glu Ser Phe Phe
1 5

(2) INFORMATION FOR SEQ ID NO:145:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS148 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:145:

GCGGACCCGT GGCTACTC
18

(2) INFORMATION FOR SEQ ID NO:146:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS148 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:146:

Ala Asp Pro Trp Leu Leu
1 5

(2) INFORMATION FOR SEQ ID NO:147:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS149 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:147:

GCGCAGTACC CTTTCTTC
18

(2) INFORMATION FOR SEQ ID NO:148:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS149 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:148:

Ala Gln Tyr Pro Phe Phe
1 5

(2) INFORMATION FOR SEQ ID NO:149:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS150 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:149:

CCTCCGTCAT TCTTCGGC
18

(2) INFORMATION FOR SEQ ID NO:150:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS150 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:150:

Pro Pro Ser Phe Phe Gly
1 5

(2) INFORMATION FOR SEQ ID NO:151:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS151 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:151:

CTTTCCAGCC TTCCCTTC
18

(2) INFORMATION FOR SEQ ID NO:152:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS151 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:152:

Pro Ser Ser Leu Pro Phe
1 5

(2) INFORMATION FOR SEQ ID NO:153:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS152 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:153:

GACCCACCAT GGTACCTT
18

(2) INFORMATION FOR SEQ ID NO:154:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS152 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:154:

Asp Pro Pro Trp Tyr Leu
1 5

(2) INFORMATION FOR SEQ ID NO:155:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS153 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:155:

CTCTACTAAT AATAAGCA
18

(2) INFORMATION FOR SEQ ID NO:156:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS153 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:156:

Leu Tyr
1

(2) INFORMATION FOR SEQ ID NO:157:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS155 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:157:

CCTATCCCCG GTTTCACT
18

(2) INFORMATION FOR SEQ ID NO:158:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS155 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:158:

Pro Ile Pro Gly Phe Thr
1 5

(2) INFORMATION FOR SEQ ID NO:159:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS158 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:159:

TTTGACCCCT TGGGCATC
18

(2) INFORMATION FOR SEQ ID NO:160:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: LS158 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:160:

Phe Asp Pro Phe Gly Ile
1 5

(2) INFORMATION FOR SEQ ID NO:161:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS160 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:161:

CCCCCCAGTG TGAACCTC
18

(2) INFORMATION FOR SEQ ID NO:162:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS160 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:162:

Pro Pro Ser Val His Leu
1 5

(2) INFORMATION FOR SEQ ID NO:163:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(A) LIBRARY: LS161 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:163:

CCAGACAACG TCCTACCG
18

(2) INFORMATION FOR SEQ ID NO:164:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS161 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:164:

Pro Asp Asn Val Leu Pro
1 5

(2) INFORMATION FOR SEQ ID NO:165:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: Gal4 residues 89-100

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:165:

Lys Ala Leu Leu Thr Gly Leu Phe Val Gln Asp
1 5 10

(2) INFORMATION FOR SEQ ID NO:166:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS201 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:166:

TACCTTTTAC CAACCTGTAT ACCT
24
(2) INFORMATION FOR SEQ ID NO:167:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:

(B) CLONE: LS201 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:167:

Tyr Leu Leu Pro Thr Cys Ile Pro
1 5

(2) INFORMATION FOR SEQ ID NO:168:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS202 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:168:

CTACAAGTCC ACAACAGCAG ATAG
24

(2) INFORMATION FOR SEQ ID NO:169:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS202 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:169:

Leu Gln Val His Asn Ser Thr
1 5

(2) INFORMATION FOR SEQ ID NO:170:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS203 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:170:

GTTCTTGACT TCACCCCTTT CCTC
24

(2) INFORMATION FOR SEQ ID NO:171:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS203 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:171:

Val Leu Asp Phe Thr Pro Phe Leu
1 5

(2) INFORMATION FOR SEQ ID NO:172:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS205 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:172:

CCCCTTACCT ACCCCCTCGC CGGA
24

(2) INFORMATION FOR SEQ ID NO:173:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS205 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:173:

Pro Leu Thr Tyr Pro Leu Ala Gly
1 5

(2) INFORMATION FOR SEQ ID NO:174:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS206 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:174:

CTCCTCGCCT TTTACGAGAT ACCG
24

(2) INFORMATION FOR SEQ ID NO:175:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS206 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:175:

Leu Leu Ala Phe Tyr Glu Ile Pro
1 5

(2) INFORMATION FOR SEQ ID NO:176:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS207 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:176:

CCCCCTGACA CCTACATCTT CTTA
24

(2) INFORMATION FOR SEQ ID NO:177:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS207 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:177:

Pro Pro Asp Thr Tyr Ile Phe Phe
1 5

(2) INFORMATION FOR SEQ ID NO:178:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS208 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:178:

CAACTCAACT ACCCACTCGC CATA
24

(2) INFORMATION FOR SEQ ID NO:179:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS208 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:179:

Gln Leu Asn Tyr Pro Leu Ala Ile
1 5

(2) INFORMATION FOR SEQ ID NO:180:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS209 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:180:

CTCGTACTAC CCCAGCCGCA ACTC
24

(2) INFORMATION FOR SEQ ID NO:181:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS209 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:181:

Leu Val Leu Pro Gln Pro Gln Leu
1 5

(2) INFORMATION FOR SEQ ID NO:182:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:

(B) CLONE: LS212 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:182:

CCTTGGTACC CTACGCCGTA TCTG
24

(2) INFORMATION FOR SEQ ID NO:183:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS212 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:183:

Pro Trp Tyr Pro Thr Pro Tyr Leu
1 5

(2) INFORMATION FOR SEQ ID NO:184:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS215 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:184:

TGGCTCCGAT CGTTCAGCCC GTATCTG
27

(2) INFORMATION FOR SEQ ID NO:185:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS215 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:185:

Trp Leu Arg Ser Phe Ser Val Pro
1 5

(2) INFORMATION FOR SEQ ID NO:186:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS217 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:186:

CTTGAACCAT CACTATATAT GATA
24

(2) INFORMATION FOR SEQ ID NO:187:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS217 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:187:

Leu Glu Pro Ser Leu Tyr Met Ile
1 5

(2) INFORMATION FOR SEQ ID NO:188:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS218 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:188:

TGCATCTTGT CCCACCACGC TCCT
24

(2) INFORMATION FOR SEQ ID NO:189:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS218 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:189:

Cys Ile Leu Ser His His Ala Pro
1 5

(2) INFORMATION FOR SEQ ID NO:190:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS220 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:190:

GACCTCACAT GCTGTTTTTG CCTC
24

(2) INFORMATION FOR SEQ ID NO:191:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS220 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:191:

Asp Leu Thr Cys Cys Phe Cys Leu
1 5

(2) INFORMATION FOR SEQ ID NO:192:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS221 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:192:

CCGTTTATTG GCGGCCCTTA CGCA
24

(2) INFORMATION FOR SEQ ID NO:193:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS221 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:193:

Pro Phe Ile Gly Gly Pro Tyr Ala
1 5

(2) INFORMATION FOR SEQ ID NO:194:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS223 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:194:

TACCTACTAC CTTTCCTTCC GTAC
24

(2) INFORMATION FOR SEQ ID NO:195:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:

(B) CLONE: LS223 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:195:

Tyr Leu Leu Pro Phe Leu Pro Tyr
1 5

(2) INFORMATION FOR SEQ ID NO:196:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS224 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:196:

TACCCCTGGT TTCCAGTCCC CTTA
24

(2) INFORMATION FOR SEQ ID NO:197:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS224 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:197:

Tyr Pro Trp Phe Pro Val Pro Phe
1 5

(2) INFORMATION FOR SEQ ID NO:198:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS225 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:198:

TATTTACTAC CTCTCCTCTC CACT
24

(2) INFORMATION FOR SEQ ID NO:199:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS225 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:199:

Tyr Phe Leu Pro Leu Leu Ser Thr
1 5

(2) INFORMATION FOR SEQ ID NO:200:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS226 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:200:

CTCTCCATTC AACCCTATTT TTTT
24

(2) INFORMATION FOR SEQ ID NO:201:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS226 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:201:

Leu Ser Ile Gln Pro Tyr Phe Phe
1 5

(2) INFORMATION FOR SEQ ID NO:202:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS228 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:202:

GCCCTATTCT ACCTCCTCTA AAAG
24

(2) INFORMATION FOR SEQ ID NO:203:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS228 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:203:

Ala Leu Phe Tyr Leu Leu
1 5

(2) INFORMATION FOR SEQ ID NO:204:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS230 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:204:

CCNTGGCCCT ACTATTTNCC GATC
24

(2) INFORMATION FOR SEQ ID NO:205:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS230 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:205:

Pro Trp Pro Tyr Tyr Phe Pro Ile
1 5

(2) INFORMATION FOR SEQ ID NO:206:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS231 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:206:

CCGATTTGGC AATATACCAT TTTC
24

(2) INFORMATION FOR SEQ ID NO:207:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS231 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:207:

Pro Ile Trp Gln Tyr Thr Ile Phe
1 5

(2) INFORMATION FOR SEQ ID NO:208:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS232 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:208:

TTATCCCCCA CCTTTTGGGC ATTC
24

(2) INFORMATION FOR SEQ ID NO:209:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS232 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:209:

Phe Ser Pro Thr Phe Trp Ala Phe
1 5

(2) INFORMATION FOR SEQ ID NO:210:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS233 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:210:

GACCCCCCCT ACGCCTATAC TCTG
24

(2) INFORMATION FOR SEQ ID NO:211:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS233 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:211:

Phe Pro Pro Tyr Ala Tyr Thr Leu
1 5

(2) INFORMATION FOR SEQ ID NO:212:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS235 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:212:

CCTGCACTCC TGTTTCCATT CATC
24

(2) INFORMATION FOR SEQ ID NO:213:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS235 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:213:

Pro Ala Leu Leu Phe Pro Phe Ile
1 5

(2) INFORMATION FOR SEQ ID NO:214:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS236 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:214:

TTCACCTACG CTCTCCCCTT CCCC
24

(2) INFORMATION FOR SEQ ID NO:215:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS236 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:215:

Phe Thr Tyr Ala Leu Pro Phe Pro
1 5

(2) INFORMATION FOR SEQ ID NO:216:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS239 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:216:

CTCTTACCAC TGCCTCTCTT CCTC
24

(2) INFORMATION FOR SEQ ID NO:217:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS239 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:217:

Leu Phe Pro Leu Pro Leu Phe Leu
1 5

(2) INFORMATION FOR SEQ ID NO:218:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS240 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:218:

CTATTCCCCT GGACATACCA ACTT
24

(2) INFORMATION FOR SEQ ID NO:219:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS240 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:219:

Leu Phe Pro Trp Thr Tyr Gln Leu
1 5

(2) INFORMATION FOR SEQ ID NO:220:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS241 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:220:

CTTATTATGA ACTGGCCTAC ATAT
24

(2) INFORMATION FOR SEQ ID NO:221:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS241 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:221:

Leu Thr Met Asn Trp Pro Thr Tyr
1 5

(2) INFORMATION FOR SEQ ID NO:222:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS243 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:222:

TATATTTTCN CGCTGAGCTT ATCA
24

(2) INFORMATION FOR SEQ ID NO:223:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS243 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:223:

Tyr Ile Phe Leu Ser Phe Ser
1 5

(2) INFORMATION FOR SEQ ID NO:224:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(vii) IMMEDIATE SOURCE:
(A) LIBRARY: LS244 DNA SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:224:

CTAACACCCC TCCCCTCATG GCTA
24

(2) INFORMATION FOR SEQ ID NO:225:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: LS244 AMINO ACID SEQUENCE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:225:

Leu Thr Pro Leu Pro Ser Trp Leu
1 5

(2) INFORMATION FOR SEQ ID NO:226:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: First randomized LS201

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:226:

Leu Ile Cys Tyr Pro Leu Pro Thr
1 5

(2) INFORMATION FOR SEQ ID NO:227:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: Second randomized LS201

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:227:

Ile Pro Leu Tyr Leu Thr Cys Pro
1 5

(2) INFORMATION FOR SEQ ID NO:228:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: Gal4(91-100)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:228:

Ala Leu Leu Thr Gly Leu Phe Val Gln Asp
1 5 10

(2) INFORMATION FOR SEQ ID NO:229:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: First truncation of Gal4(91-100)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:229:

Ala Leu Leu Thr Gly Leu Phe Val Gln
1 5

(2) INFORMATION FOR SEQ ID NO:230:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: Second truncation of Gal4(91-100)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:230:

Ala Leu Leu Thr Gly Leu Phe Val Asp
1 5

(2) INFORMATION FOR SEQ ID NO:231:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: Third truncation of Gal4(91-100)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:231:

Ala Leu Leu Thr Gly Leu Phe Gln Asp
1 5

(2) INFORMATION FOR SEQ ID NO:232:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: Fourth truncation of Gal4(91-100)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:232:

Ala Leu Leu Thr Gly Leu Val Gln Asp
1 5

(2) INFORMATION FOR SEQ ID NO:233:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: Fifth truncation of Gal4(91-100)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:233:

Ala Leu Leu Thr Gly Phe Val Gln Asp
1 5

(2) INFORMATION FOR SEQ ID NO:234:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: First modification of Gal4(91-100)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:234:

Ala Leu Leu Thr Gly Leu Phe Val Gln Ala
1 5 10

(2) INFORMATION FOR SEQ ID NO:235:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: Second modification of Gal4(91-100)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:235:

Ala Leu Leu Thr Gly Leu Phe Val Ala Asp
1 5 10

(2) INFORMATION FOR SEQ ID NO:236:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: Third modification of Gal4(91-100)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:236:

Ala Leu Leu Thr Gly Leu Phe Ala Gln Asp
1 5 10

(2) INFORMATION FOR SEQ ID NO:237:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(vii) IMMEDIATE SOURCE:
(B) CLONE: Fourth modification of Gal4(91-100)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:237:

Ala Leu Leu Thr Gly Leu Ala Val Gln Asp
1 5 10

(2) INFORMATION FOR SEQ ID NO:238:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 13 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:238:

Leu Phe Val Gln Asp Tyr Leu Leu Pro Thr Cys Ile Pro
1 5 10

Claims